

FOOD SYSTEM CONTRIBUTIONS TO BISPHENOL-A EXPOSURES

by
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Abstract

This dissertation explores the food system's contributions to bisphenol-A (BPA) exposures through an analysis of dietary data, modeling of the potential BPA exposure from school meals, and a review of food contact materials policies. Its discoveries enhance the epidemiologic work examining sources of bisphenol A exposures from the food system to inform and improve policy.

Data from NHANES 2003-2008 were utilized to identify dietary contributions associated with the presence of bisphenol-A in humans. Statistical analysis modeled relationships between urinary BPA concentrations and consumption of canned food and beverages, as identified by 24-hour dietary recall, accounting for demographic and socioeconomic factors. In addition, factor analysis methods were conducted to discover dietary patterns associated with higher urinary BPA concentrations. The regression models revealed a statistically significant increase in urinary BPA concentration with greater consumption of canned food, and specifically canned pasta, vegetables, and beans. The exploratory factor analysis revealed that the dietary patterns of the population with the highest urinary BPA concentrations differed from the other population categories explored, giving evidence that specific food groups could be contributing to higher BPA exposures.

The school meal exposure models forecasted potential daily doses of bisphenol-A from a typical school breakfast and lunch based on different exposure scenarios. Values ranged from 7.7×10^{-4} $\mu\text{g/kg-BW/day}$ to $0.97 \mu\text{g/kg-BW/day}$. The modeled BPA exposure doses are low in comparison to the BPA RfD of $50 \mu\text{g/kg-BW/day}$ determined

by the EPA to be a safe chronic exposure level. Newer research performed since the RfD was established demonstrates that the threshold for animal toxicity to BPA is as low as 0.025 µg/kg-BW/day. Many of the doses modeled exceed this toxicity threshold, illustrating the potential for school meals to place children at risk for toxic exposures of BPA.

This research confirmed the need for more investigations of BPA in institutional food. Efforts should focus on laboratory analysis for BPA in foods unique to schools, such as institutional sized cans, bulk bags of frozen, pre-cooked proteins, and individually wrapped foods. Additional research should quantify the transfer of BPA from food preparation and service activities.

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CHAPTER ONE: Introduction

Bisphenol-A Background

Bisphenol-A (BPA) is an organic compound, first synthesized by a Russian scientist named A.P. Dianin in 1891 (Rubin 2011). In the 1930's, its estrogenic properties were discovered when scientists conducted BPA feeding experiments on ovariectomized rats. At this time, it was screened as a possible synthetic estrogen replacement (Cavalieri and Rogan 2010). Although BPA expresses estrogenic properties, it is 10,000 to 100,000 times weaker than estradiol in its affinity for traditional estrogen receptors pathways (Vandenberg et al. 2007). Due to this, the pharmaceutical industry chose another synthetic estrogen, diethylstilbestrol, or DES, for use with pregnant women to prevent miscarriage and premature birth (Rubin 2011). DES is now an infamous illustration of the harmful effects of endocrine disruption. Fetal exposure to DES is capable of causing offspring to develop reproductive issues and post pubertal female offspring to develop a rare clear-cell carcinoma.

BPA did not remain unutilized for long; its usefulness as a building block for consumer products was soon discovered. BPA has two phenol functional groups that are well suited for use as a monomer base for polycarbonate plastic (PC). PC is widely used due to its durability, shatter resistance, transparency, thermostability, and lightweight nature. BPA is additionally used as a linkage in manufacturing epoxy resins, compounds that provide corrosion resistance, flexibility, and heat resistance. BPA is also employed as a color developer in thermal receipts (Geens et al. 2012; Liao and Kannan 2011), as a

component of dental composites (Joskow et al. 2006; Olea et al. 1996) , and in medical devices (Calafat et al. 2009).

The use of polycarbonate plastics and epoxy resins in many consumer products has led to the annual manufacturing of over six billion pounds of BPA, making it one of the world's highest production volume chemicals (Melzer et al. 2010; Willhite et al. 2008). Due to its widespread use, BPA has been detected in household dust and air (Wilson et al. 2007) and in water contaminated by landfill leachate and wastewater effluent (Tsai 2006; Vandenberg et al. 2007; vom Saal et al. 2007). It is also found in detectable levels in a variety of paper products, unintentionally incorporated into goods during the recycling process (Geens et al. 2012; Liao and Kannan 2011; Ozaki et al. 2004). Recycled paper products contain ten times more BPA than virgin paper products. The source of BPA in recycled products can be traced back to thermal receipts with BPA being introduced into the recycling stream (Ozaki et al. 2004).

With so many contributing sources, BPA exposure in the human population is ubiquitous. BPA has been measured in the urine of 92.6 % of the American population (Calafat et al. 2008). Although BPA exposure contributions include many sources, diet is the main contributor of BPA exposure (Kang et al. 2006; von Goetz et al. 2010; Wilson et al. 2007).

BPA in the Food System

BPA was first approved for use in food packaging in the 1960's (FDA 2012a). In the food system, BPA is mainly found in polycarbonate (PC) plastic containers and in the epoxy resin lining of food and beverage containers. Epoxy resin coatings are found in traditional canned foods, as well as pre-prepared infant formula, on the inside of jar lids, and on the inside of aluminum beverage containers such as soda and beer cans. The purpose of can coating is to protect the metal can from corrosion which could allow microbes to enter its contents. Can linings are also added in order to protect food from acquiring a metallic taste and to maintain food's color and texture. Additional performance requirements of can coatings are that they have to be able to withstand the stresses of food processing including can distortion and high temperature sterilization, as well as bending and dinging, without degrading or separating off of the metal can walls (Lakind 2013; Noonan et al. 2011).

Polycarbonate plastics containing BPA are frequently used in consumer products that are in contact with foods. They can be commonly found in plastic serving dishes, plastic serving utensils, temporary food storage containers such as Tupperware, and reusable water bottles. Although no longer approved for use in infant feeding systems since a July 2012 ruling by the FDA, at the time of the NHANES studies from 2003-2008 utilized in this research, BPA could be commonly found in PC baby bottles and sippy cups (FDA 2012b).

The concern of using BPA in food packaging stems from its propensity to leach into the product. In 1993, scientists accidentally discovered BPA leaching from their polycarbonate lab ware into experimental media. During their trials, they mistakenly

believed that the substance competing with estradiol for estrogen receptors was the yeast culture they were testing. Upon closer investigation, they identified the estrogenic substance as BPA that had migrated into the distilled water of their experimental culture media when it was autoclaved in polycarbonate flasks (Krishnan et al. 1993). This confirmed that BPA leaches from polycarbonate plastic and that it demonstrates estrogenic properties.

Multiple studies have shown that BPA can leach from polycarbonate baby bottles during normal use activities such as cleaning in a dishwasher, boiling, and brushing (Brede et al. 2003). Besides polycarbonate materials, studies have shown BPA leaching from polyvinyl chloride (PVC) stretch films, or plastic cling wrap, during simulation tests with water, acetic acid, and olive oil. BPA leached from the PVC films into the food simulants at migration rates higher than many other food contact materials (Lopez-Cervantes and Paseiro-Losada 2003).

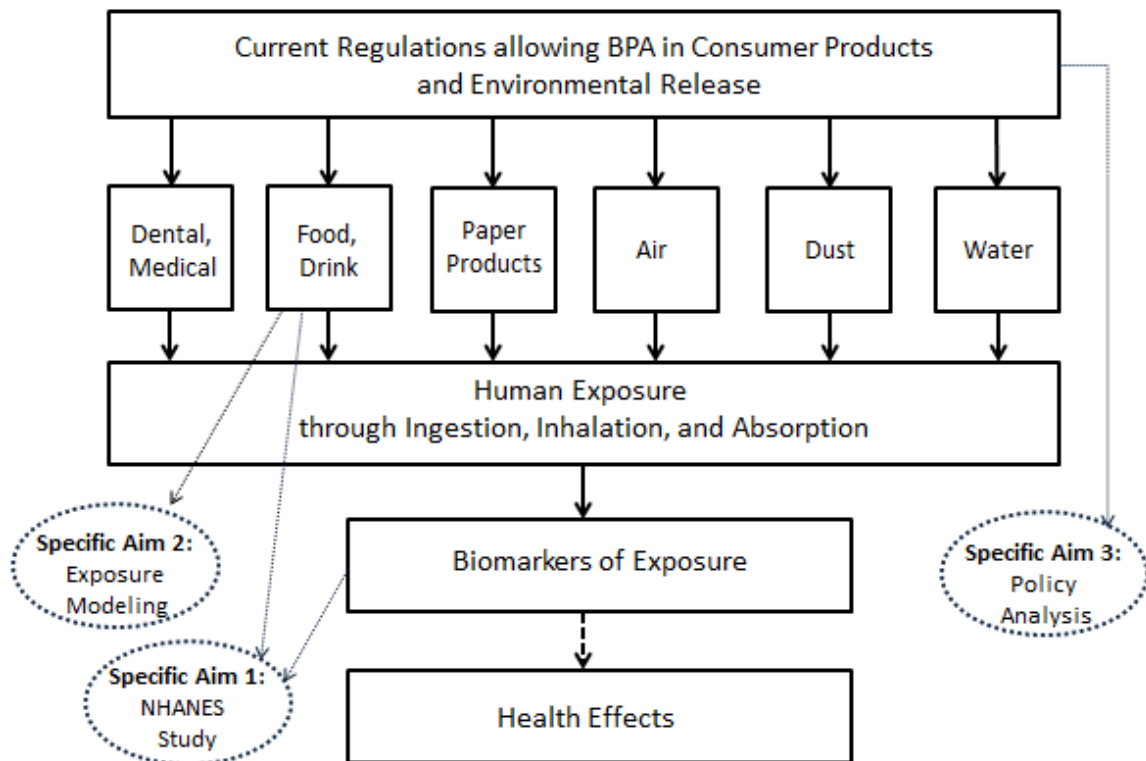
BPA, a monomer, does not completely polymerize in the manufacturing of epoxy resins, leaving free BPA molecules to migrate from the resin into the food (McNeal et al. 2000; Oldring and Nehring 2007). It was first documented that BPA migrates from epoxy resin lining of canned food into its products by Brotons. In this migration study, the aqueous portion of canned vegetables was analyzed as well as water autoclaved in these same cans. All of the hormonal activity measured from these liquids was attributable to Bisphenol-A (Brotons et al. 1995).

Research Aims

This research's overall aim is to explore the dietary exposure pathway of BPA.

Figure 1.1 is a conceptual model of BPA exposure that illustrates where my research aims fit into the overall BPA exposure framework. **Specific Aim 1** is to use NHANES data to examine dietary sources of differential BPA exposure by gender, age, race/ethnicity, income levels, education levels, and smoking status. **Specific Aim 2** is to model potential BPA exposure contributions from school nutrition services. **Specific Aim 3** is to discuss the public health implications and policy opportunities from research findings.

Figure 1.1: Research Aims in BPA Exposure Framework



Research Overview

The research studies included in this dissertation examine the sources of BPA exposures from the food system. Chapter Two, entitled “Literature Review of Bisphenol-A in the Food System,” explores published works on BPA, focusing on the breadth of its exposure pathways, its metabolism, health effects, risk characterization, food contact materials policies, and the feasibility of removing BPA from the food system. Chapter Three is Manuscript 1 entitled, “An evaluation of urinary BPA concentrations and the consumption of canned foods using NHANES 2003-2008.” This research project was designed to examine the consumption of canned food and beverages and identify whether consumption of these types of packaged food contributed to high concentrations of BPA in the body. In order to identify dietary contributions, there was a focus on the diet of study subjects in the 24-hour exposure window prior to urinary BPA concentration testing. The goal of this research project is to identify the dietary contributions that can be associated with the highest bisphenol-A concentration levels in humans. One specific research aim is to seek associations between urinary BPA concentrations and consumption of canned food and beverages, as identified by 24-hour dietary recall, and accounting for demographic and socioeconomic factors. This study’s second aim seeks to identify dietary patterns of the participants, comparing the whole population with the subpopulations of participants with the highest urinary BPA concentrations and the lowest urinary BPA concentrations in order to identify eating patterns that could put people at risk for high BPA exposure.

In Chapter Four, Manuscript 2 is entitled, “Formative Research to inform BPA Exposure Models of School Meals.” This chapter describes the formative research

conducted to develop the BPA potential exposure models in school meals. Research for this project included interviews with key food service personnel, school cafeteria and kitchen site visits, a food service director survey, and a literature review.

Chapter Five, Manuscript 3 is entitled, “Probabilistic Modeling of School Meals for Potential BPA Exposure.” This research project conducts exposure modeling utilizing deterministic and probabilistic methods. The goal of this research is to model the potential bisphenol-A exposure dose of a school meal from a typical public school that participates in the National School Lunch Program and School Breakfast Program. These daily doses will then be compared to the allowable dose of 50 µg/kg-BW/day determined by the EPA to be a safe chronic exposure level for BPA.

Chapter Six is entitled, “Policy and Advocacy Directions to Reduce BPA Exposures.” This chapter reviews the current food contact materials and other governmental policies that allow BPA exposures, mainly from the food system. The changes needed to inform and facilitate policy reform are then described. The chapter is organized into policy perspectives of food contact materials regulations, non-dietary BPA exposures, grass roots and consumer advocacy approaches, the United States government’s position on BPA, scientific research opportunities, and government policy reform.

In the final chapter, conclusions are made about the NHANES dietary study, the school food exposure assessment, and the policy implications of each research study. This chapter additionally describes the future research needs and next steps in the field of BPA and endocrine disrupting chemicals.

Prior to commencing this research, the project protocol was submitted to the Institutional Review Board of the Johns Hopkins Bloomberg School of Public Health. The research was determined to be “Not Human Subjects Research” and did not require a full review from the Institutional Review Board.

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CHAPTER TWO: Literature Review of Bisphenol-A in the Food System

BPA in the Food System

After Bisphenol-A (BPA) was first documented to migrate from epoxy resin lining of canned food into its products in 1995 (Brotons et al. 1995), a significant body of work about the leaching of BPA into canned food has been performed by scientists worldwide. One of the early studies analyzing canned food contents was conducted in Goodson's laboratory in 2002. Sixty-two different canned foods were purchased from retail outlets in the United Kingdom. The can contents were homogenized before analysis by GC-MS. BPA was found at detectable levels in more than half of the foods (Goodson et al. 2002). Goodson's research team also studied the effects of damage to canned foods and storage time on the release of BPA into the food. In their analysis, they discovered that the foods and simulants acquired 80-100% of the total BPA present in the can coatings immediately after the sealing and sterilization processes. Denting of the cans did not increase the migration of BPA into food. After heating the food while it was still inside the can in boiling water, as one might do to prepare the food for consumption, no increase in BPA migration was seen. Allowing canned products to be stored for the entire shelf-life also does not increase BPA levels in the foodstuffs (Goodson et al. 2004).

In 2005, Thomson and Grounds conducted an exposure assessment of eighty different canned foods from retail outlets in New Zealand. They detected BPA in all of the foodstuffs except soft drinks. The highest concentrations of BPA were found in canned tuna, corned beef, and coconut cream. As part of their assessment, they constructed exposure doses by using the mean BPA concentration determined from their

food testing and 24-hour dietary recall information from over 4000 individuals. The mean exposure dose was determined to be 0.008 µg/kg BW/day and the maximum exposure was 0.29 µg/kg BW/day. Most of the individual scenarios that they modeled resulted in no BPA exposure. These exposure doses were based on adult consumption scenarios, and, therefore, cannot be used to make conclusions about exposures of other age groups (Thomson and Grounds 2005).

Vivacqua's study conducted in Italy is one of the few studies that investigated the BPA content of fresh fruit and vegetables. Fourteen fresh foods were selected for analysis for the presence of BPA and nonylphenol. BPA concentrations were discovered in eight of the fourteen fresh foods in the range of 0.25 to 1.11 mg/kg. The study also explored the estrogenic activity of the contaminants. Estrogen-like activity was displayed in their tests with the estrogen dependent MCF7 breast cancer cells (MCF7wt), its hormone dependent but ER α -positive variant MCF7SH, and the steroid-receptor- negative human cervical carcinoma HeLa cells (Vivacqua, et al. 2003).

BPA studies from North America

In North American studies of BPA in canned food, the majority of Canadian research has been conducted by the Food Research Division in the Bureau of Food Safety of Health Canada. This research has been used by Health Canada to estimate the Canadian population's exposure to BPA (Bureau of Chemical Safety 2010; Cao et al. 2010). Estimation of food sources of BPA in Canada included an analysis of 78 canned foods purchased in Ontario, Canada. The overall findings showed that canned tuna had the highest BPA concentrations, condensed soup concentrations were greater than ready-

to-serve, canned vegetables had very low BPA concentrations, and that canned tomato paste products had lower BPA concentrations than canned pure tomato products (Cao et al. 2010). The same research group also completed research in estimating the BPA exposure from total diet studies. This entails making food composites by combining different forms of the same food, such as frozen and canned corn, to represent the variety of foods available in the marketplace. In making the food composites, the ability to determine the BPA concentration from a specific source is lost. This total diet study was conducted with foods from Quebec City. After analysis of the food, this research modeled BPA dose for different age-sex groups. Infants had the highest exposure per kilogram body weight, with a modeled exposure of 0.17 -0.33 $\mu\text{g/kg-BW/day}$ as compared to 0.052 -0.081 $\mu\text{g/kg-BW/day}$ for adults. The majority of BPA exposures could be traced to intakes from 19 of the 55 samples. Most of these samples were from canned or jarred food (Cao et al. 2011). The Food Research Division has also studied canned beverages, including soft drinks and beer. This research showed that overall there are low to non-detectable levels of BPA found in soft drinks packaged in plastic or glass and beer packaged in glass. The same types of beverages, packaged in cans, contain low concentrations of BPA (Cao et al. 2010; Cao et al. 2009).

In the Dallas, Texas area of the United States, Schecter's laboratory purchased 105 fresh foods and foods packed in plastic or cans for BPA analysis. Included in this sample are cat and dog foods that came in plastic and can packaging. BPA was detected in 63 of the 105 samples. The highest BPA concentration was found in canned Del Monte Fresh Cut Green Beans. Only one fresh food item, sliced turkey, had detectable concentrations of BPA (Schecter et al. 2010).

Another U.S. study was conducted by Noonan's laboratory in the Center for Food Safety and Applied Nutrition of the USDA in 2011 using foods purchased in the Maryland and DC area. Using sales data, this study selected sixteen different food types that constituted 65% of the canned food consumed in the U.S. Only the edible portions, or the solid food contents, were analyzed for BPA in this experiment. Analysis showed that fruits and tuna displayed the lowest BPA concentrations. BPA was found at low to non-detectable levels in canned fruit, confirming that a general industry practice is to use unlined tin can bodies with lined ends and seams for canned fruit containers (Oldring and Nehring 2007). Overall, this study showed a great variability in BPA concentrations among the food products of the same type of food and among different lots of the same food product (Noonan et al. 2011).

In research from Mexico, Munguia-Lopez's laboratory studied the relationship between heat processing and storage time and the amount of BPA leaching from can linings. This study was limited to investigating two types of food common to the Mexican diet: canned tuna fish and jalapeño peppers. Each can has a different type of can lining: tuna cans were coated with organosol, a polyvinyl chloride derived resin, and jalapeño pepper cans were coated with an epoxy resin. Organosol coatings do not contain BPA by themselves. The common practice of adding bisphenol A diglycidyl ether (BADGE) to scavenge for excess hydrogen chloride is usually the source of BPA residues (Goodson et al. 2002). This study utilized empty cans provided by the manufacturer, placed distilled water as an aqueous food simulant into the cans, and sealed them. Both types of cans were heat processed in the same manner as during regular manufacturing. The jalapeño peppers, due to their high acidity, are processed at 100°

Celsius for 9 minutes and tuna needs to be processed at 121° Celsius for 90 minutes. The heat processing to 121° Celsius performed with the tuna's fatty-food simulant elevated the migration of BPA. The storage time affected the jalapeño pepper cans but not the tuna fish cans (Munguia-Lopez and Soto-Valdez 2001).

Munguia-Lopez also conducted similar experiments with tuna and vegetable cans with organosol, epoxy resin, and organosol and epoxy resin linings. The experiments were performed according to European and Mercosur regulations. In this research, they tested for BPA migration using sunflower oil as a fatty food simulant. It was discovered that BPA migrated into this fatty food simulant at a higher rate than the aqueous food simulant after heat processing. When cans were not heat processed, BPA migration increased with longer storage time. For cans that were heat processed, BPA migration was very high from the heating. As the cans remained in storage, the BPA levels actually decreased. Their hypothesis is that the BPA acted as an antioxidant for the sunflower oil, decreasing BPA levels as reactions occurred over time. Different levels of BPA migrations were also shown between different can batches of the same type of coating (Munguia-Lopez et al. 2005).

BPA Studies from Asia

Japanese scientists have performed extensive research on BPA in the food system. Yoshida performed some of the earliest work from Japan. Yoshida's laboratory developed methods for detecting BPA in canned food samples of homogenized canned contents and the aqueous portion of the cans. They also performed partitioning experiments. Their research discovered that BPA first migrates from the can lining into

the aqueous portion of the contents during the canning process. As the canned foods are stored, the BPA will then migrate into the solid portions. BPA was detected in significantly higher quantities in the solid portion of the can contents than the aqueous portion (Yoshida et al. 2001). In further Japanese studies, Yonekubo's laboratory investigated BPA concentrations in 38 different canned foods. The canned food contents were homogenized before analysis with LC-MS/MS. Their research found a difference in BPA concentrations depending on the can style. For example, cans with easy pull off lids have ten times more BPA leaching into the food than the traditional cans (Yonekubo et al. 2008). In Sajiki's laboratory, BPA tests were performed on 87 regularly consumed foods packaged in cans, plastic, and paper. High levels of BPA were detected in canned vegetables, soups, and sauces. No BPA was detected in their canned fruit. Fresh strawberries from plastic packaged were also tested and BPA was detected. The researchers believe that the BPA detected in the fresh strawberry is from the plastic used in the growing stages of the strawberry and not from the packaging (Sajiki et al. 2007).

In a Korean study investigating the BPA content of canned foods, 61 canned food items were purchased. Of the 61 food items, 39 had detectable levels of BPA ranging from 3.28 to 136.14 $\mu\text{g/kg}$. The highest BPA concentrations were found in canned tuna, with an average of 43.7 $\mu\text{g/kg}$, and coffee, with an average of 45.51 $\mu\text{g/kg}$. Fruits and vegetables were the most likely to have non-detectable levels of BPA. Their modeled daily intake of BPA was 1.509 $\mu\text{g/kg-BW-day}$ (Lim et al. 2009).

BPA from Non-Food Exposure Pathways

Although BPA exposures from dietary sources are the primary pathway, detectable levels of BPA can be found in soil, dust, air, water, and medical devices leading to exposure from inhalation and dermal absorption pathways (Kang et al. 2006; von Goetz et al. 2010; Wilson et al. 2007).

Occupational exposure to BPA mostly occurs through the inhalation and dermal pathways. Workers could be exposed during the manufacturing of BPA monomers, while BPA is being incorporated into commercial products such as epoxy resin powder paint, and throughout packaging and transport. It is possible to be exposed to BPA during the thermal processing used to recycle plastics and make them into new commercial products (Tsai 2006). Cashiers who frequently handle thermal receipts are at greater risk for BPA exposure. In models of exposure to BPA from daily intake and dermal absorption, occupationally exposed individuals were dosed at rates 100 times the general population (Liao and Kannan 2011). In a study of the urinary BPA concentrations of pregnant women, cashiers were the occupational category most highly exposed. This study revealed an additional source of BPA exposure: smoking. Women who actively smoked or were exposed to secondhand smoke had 20% higher urinary BPA concentrations than non-smokers. The BPA exposure is likely from the tobacco smoke that becomes contaminated from the BPA-laden filter. Some cigarette filters are as much as 25% BPA by weight (Braun et al. 2011).

BPA levels in the air, water, and soil environments have been detected and should be closely monitored. It is known that BPA is released into the environment. According to the Toxics Release Inventory (TRI), 1.8 million pounds of BPA was released into the

environment in 2003 in the United States. This waste was released from the industrial sector, municipal wastewater treatment plants, and landfills (Tsai 2006). The EPA states that a million pounds of BPA are released into the environment (EPA 2012a).

Although BPA is known to be released into the air from TRI reports and has been measured in outdoor and indoor air, BPA's physical properties of a high boiling point and low vapor pressure do not allow BPA to easily evaporate. From this information, some scientists conclude that BPA inhaled from the air should not be of concern as an exposure route (Kang et al. 2006; Sajiki et al. 2007). Of the BPA releases reported through TRI in 2003, 123,000 pounds were released to the air. This is a small amount compared to the overall releases of BPA to the environment (Tsai 2006). In outdoor air, BPA's concentration ranges from <0.1 and 4.72 ng/m^3 . In indoor air, BPA concentration is much higher, with a range of <0.1 to 29.0 ng/m^3 . BPA levels in the air are from several sources. Indoor sources of BPA are hypothesized to be from household goods and furniture (Wilson et al. 2001; Wilson et al. 2003). Outdoor concentrations of BPA may be from combustion by-products such as from open-air barrel burns that total 79,000 kg per year (Sidhu et al. 2005).

Studies of BPA in the aquatic environment are numerous. BPA has been detected in leachates from industrial and municipal waste disposal sites at $8400 \mu\text{g/l}$ and $10,300 \mu\text{g/l}$, respectively. These levels are higher than aquatic toxicity value. BPA can also be detected in wastewater effluents from paper recycling plants (Fukazawa et al. 2001). BPA is considered to be readily biodegradable by bacteria in rivers under aerobic conditions with a half-life in freshwater of 3-5 days. In seawater, BPA persists much longer, about thirty days. In both aquatic environments, the aquatic organisms have been shown to have

higher levels of BPA in their systems than is measurable in their aqueous environment. Caution should be taken in consuming seafood and freshwater fish from contaminated waters (Kang et al. 2006). Due to the way that drinking water is treated, through chlorination, ultraviolet light radiation, and ozonation, estrogenic compounds are destroyed. Even if BPA does leach from a PVC pipe, it will be destroyed by the chlorine in the water (Lee et al. 2004; Sajiki and Yonekubo 2002).

Sediment can serve as a sink for BPA contamination due to BPA's organic carbon partition coefficient tested in the range of 2.5 to 4.64 (Staples et al. 1998). Soil and sediment samples from rivers in Taiwan and Germany show that BPA concentrations are higher in the soil than the water, showing evidence of its partitioning into the soil (Heemken et al. 2001; Lin 2001; Stachel et al. 2005).

BPA is a component of dental composites and sealants. In a study of BPA residue after application of composite resins containing BPA, saliva was analyzed before treatment, after treatment, and after gargling. Saliva samples were collected after a patient chewed on a paraffin pellet for five minutes. BPA was detectable in the saliva directly after treatment, but was easily removed after gargling with tepid water for thirty seconds. BPA exposure from this route is therefore not chronic (Sasaki et al. 2005). Exposure assessment research was conducted on patients receiving dental sealants containing BPA. Only one of the two brands of sealants leached significant levels of BPA, on the same level where estrogen receptor –mediated effects have been seen in laboratory animal tests. Urinary BPA concentrations remain elevated for more than 24 hours (Joskow et al. 2006).

There is concern over possible BPA exposure from the plastic components of medical devices and equipment. Polyvinyl chloride (PVC) plastics are known components of medical tubing and bags. PVC is a concern because it can contain BPA and phthalate additives. In a recent study of premature infants that have received medical treatment in the neonatal intensive care unit, researchers classified babies into risk categories according to their degree of exposure to PVC plastic medical devices containing di(2-ethylhexyl) phthalate (DEHP). It was found that babies that received the most intensive care had an order of magnitude higher urinary BPA concentration than the general population (Calafat et al. 2009)

BPA in the Human Population: Biomonitoring

BPA has been detected in the human body in blood, urine, saliva, breast milk, semen, amniotic fluid, and follicular fluid (Vandenberg et al 2007, 2010). Since BPA can be found in nearly the whole population at any given time even though it is rapidly metabolized, it is believed that human exposure to BPA must be significant, continuous, and from multiple sources (vom Saal and Hughes 2005).

A valuable tool in researching associations of BPA body burdens with socioeconomic factors and adverse health outcomes in the United States population is the National Health and Nutrition Examination Survey, or NHANES. NHANES is a continuous, cross-sectional study that uses a complex, multi-stage sample design to achieve nationally representative samples. It entails dietary assessments, physical examinations, and laboratory testing. Data analysis and reporting of the laboratory testing performed in NHANES is completed by the Centers for Disease Control's Environmental Health Laboratory (CDC 2012a). The CDC publishes the National Report on Human Exposure to Environmental chemicals with the latest being the Fourth National Report released in 2009. This report includes chemicals where there is concern of exposure and health effects (CDC 2009).

Starting in 2003-2004, Bisphenol A has been tested in NHANES in a representative random, one-third subsample of NHANES participants 6 years and older. In this NHANES cycle, there were 10,122 subjects in the total sample and 2517 in the subsample. Of the 2517 participants in this subset, urinary BPA concentrations were detected in 92.6% of this population. The unadjusted geometric mean urinary BPA concentration for 2003-2004 was 2.49 ng/ml (95% CI of 2.2 to 2.83) (Calafat et al. 2008).

Children have the highest urinary BPA concentrations of the ages tested in NHANES. An analysis of NHANES 2003-2004 data showed that the BPA concentration of 6-11 year olds, adjusted for sex, race/ethnicity, age group, creatinine concentration, and income, had a least squares geometric mean (LSGM) of 4.5 µg/l (95% CI of 3.9 to 5.1). The urinary BPA concentrations of this age group were statistically significantly higher than adolescents' ages 12-19 years old ($p < 0.001$). The adolescents, in turn, had higher BPA concentrations than adults ($p < 0.001$) (Calafat et al. 2008).

In the 2005-2006 NHANES cycle, the unadjusted geometric mean urinary BPA concentration declined to 1.79 ng/ml (95% CI of 1.64 to 1.96) (Melzer et al. 2010). In this same cycle, research was conducted to estimate BPA intakes derived from the NHANES individual urinary BPA concentrations and individual body weights. These calculations found the highest BPA median intakes in its youngest age groups, the 6-11 year olds, with an intake of 64.6 ng/kg-day, and 12-19 year olds, with an intake of 71.0 ng/kg-day. Each subsequent age category had decreasing median BPA intakes: 52.9 ng/kg-day for 20-39 year olds, 38.3 ng/kg-day for 40-59 year olds, and 33.5 ng/kg-day for subjects sixty years and older (Lakind and Naiman 2011).

Analysis of the 2003-2004 NHANES data showed that urinary BPA concentrations varied by race/ethnicity. Race/ethnicity was stratified into three categories: non-Hispanic Whites, non-Hispanic Blacks, and Mexican-Americans. In studies by Calafat, the analysis found that Mexican-American urinary BPA least squares geometric mean (LSGM) concentration of 2.3 µg/l was statistically significantly lower than non-Hispanic Blacks (3.0 µg/l) and non-Hispanic Whites (2.7 µg/l). There was no statistical difference between non-Hispanic Blacks and non-Hispanic Whites (Calafat et

al. 2008). Lakind and Naiman's use of 2005-2006 NHANES data to compare BPA intakes according to ethnicity similarly found that Mexican-Americans and Non-Hispanic Whites had statistically significantly lower urinary BPA than non-Hispanic Blacks (Lakind and Naiman 2011).

Income analysis of the 2003-2004 NHANES showed that BPA exposures are highest for those with the lowest income bracket. In regression models of urinary BPA concentrations including the variables of sex, race/ethnicity, age group, creatinine concentration, and income, the adjusted LSGM was statistically significantly higher for the low household income category of <\$20,000 (3.1 µg/l) as compared to high household income of > \$45,000 (2.5 µg/l) (Calafat et al. 2008). In a recent study of NHANES cycles 2003-2008, an association was found showing families with lower income, lower food security, and that accessed emergency food assistance had higher urinary concentrations of BPA (Nelson et al. 2012).

The evidence for differences in BPA exposure levels by sex is not consistent among studies. In Lakind and Naiman's studies of NHANES 2003-2004 and 2005-2006, modeled median daily intake of BPA exposures for males is higher than for females (Lakind and Naiman 2008; Lakind and Naiman 2011). In Calafat's research, their regression model on BPA urinary biomarkers for NHANES 2003-2004 found exposures for females higher than males (Calafat et al. 2008). In a small scale longitudinal study of Japanese schoolchildren, no statistically significant difference in BPA exposure levels was found between boys and girls (Yamano et al. 2008).

NHANES dietary assessment tools were analyzed for indicators of dietary exposures that may lead to high urinary BPA concentrations. The only question from the food frequency questionnaire (FFQ) pertaining to food packaging inquires about the consumption of canned tuna. In the dietary recall data, information is recorded on intake of bottled or canned drinks. In analysis of these two pieces of dietary information, neither of these consumption areas was found to be associated with increased urinary BPA. Urinary BPA concentrations were found to be higher for study participants that drank more soda, although the packaging of the soda consumed is unknown. From FFQ data, urinary BPA concentrations were found to be statistically significantly higher for subjects that ate more school lunches and consumed more prepared food outside of the house (Lakind and Naiman 2011).

To discover the body burden of BPA in the Asian population, Zhang's laboratory investigated urinary BPA concentrations in several Asian countries. The lab analyzed samples from 296 participants from Kuwait, Korea, India, China, Vietnam, Malaysia, and Japan. BPA was detected in 94.3% of the samples. Kuwait had the highest levels with an estimated median daily intake of BPA of 5.19 $\mu\text{g/day}$, and Japan had the lowest, with 1.61 $\mu\text{g/day}$. The age group with the highest intake were subjects less than or equal to 19 years of age. No significant gender difference was detected between subjects living in urban or rural area (Zhang et al. 2011).

BPA Metabolism in Humans

A handful of studies have researched the metabolism of BPA in humans after exposure. When BPA is ingested by humans, it is biotransformed in the liver on its first pass into bisphenol A-glucuronide, a highly water soluble metabolite. This metabolite is then rapidly excreted by the kidneys with urine (Volkel et al. 2002). By monitoring BPA doses in healthy adults from ingestion to excretion, evidence shows that BPA's half-life in the body is less than six hours and it is completely cleared from the body in 24 hours (Tsukioka et al. 2004; Volkel et al. 2002). This rapid clearance from the body through urine makes total urinary species, comprised of free plus conjugated BPA, the most appropriate BPA exposure assessment marker (Melzer et al. 2010). Dermal absorption and inhalation of BPA is of concern because exposures from these pathways are able to circumvent the first-pass metabolism of the liver and enter the circulatory system directly (Vandenberg et al. 2007).

BPA exposure in infants and children is a critical concern because their liver and kidneys are still developing. The kidneys do not reach full maturation until two years of age. In their first year, the glomerular filtration volume of the kidneys develops. In the second year, the renal tubular function that excretes toxins increases to adult capacity (Yamano et al. 2008). Due to incomplete liver maturation, infant systems are unable to metabolize BPA through glucuronidation as adults do. It is theorized that infants metabolize BPA through a combination of glucuronidation and sulfation. Research on the biotransformation of acetaminophen shows neonates rely on sulfotransferases to metabolize this drug. This mechanism for metabolizing BPA is plausible because BPA is a substrate for sulfation; and sulfotransferases, responsible for sulfation, develop earlier

in neonates than UDP-glucuronosyltransferases, responsible for glucuronidation (Ginsberg and Rice 2009).

BPA's metabolism in humans was also studied in a 36-hour dosing experiment where 10 men and 10 women ingested one of three specified meals made from grocery store food for breakfast, lunch, and dinner. Blood and urine samples were taken every hour to monitor BPA metabolism. It was discovered that serum levels of BPA were 42 times lower than in urine. Their findings closely matched the serum levels studied in Volkel's high dose studies (Volkel et al. 2002). The slight differences in timing of peak BPA in serum could be from the fact that in Volkel's study, the BPA was ingested from a hard gelatin capsule and in Teeguarden's study, the BPA dose was administered through a regular meal. The high comparability of serum pharmacokinetics between these two studies provides strong evidence that adsorption and elimination of BPA is linear in humans. This study learned that spot urine samples reflect exposures from the prior meal, in a 4-6 hour timeframe. The timing of spot urine sample in comparison to prior meals and taking into account the timing of the previous void which would eliminate accumulated BPA will also determine its ability to accurately measure exposures (Teeguarden et al. 2011).

There is some research challenging the commonly held belief that BPA exposures are almost exclusively from food sources. For NHANES, the urinary BPA concentration testing takes place after a period of overnight fasting for 9.5 hours for morning appointments and 6 hours of fasting for afternoon and evening appointments (CDC 2012b). As BPA levels remained higher than BPA half-life calculations predict, Stahlhut's study showed the possibility of people's exposure to non-food sources as

being more significant than previously estimated, in addition to the possibility that BPA is being stored in fat and slowly released (Stahlhut et al. 2009). In a study by Christensen, urinary BPA concentrations of 5 healthy individuals were monitored before, during, and after a 48 hour fasting period. The data showed that the BPA concentrations decreased significantly after 24 hours, and then remained at a constant low level for the remainder of the study. They concluded the remaining BPA concentrations are attributed to either non-dietary sources, mainly from dust, or that small reservoirs of BPA from past exposures are being released and excreted (Christensen et al. 2012).

Some research disagrees on regulatory frameworks based on the belief that rapid metabolism and excretion of BPA in humans also diminishes any concern about fetal and neonatal exposures. Regulations should consider, according to Ginsberg and Rice, the ability of fetal and neonatal deconjugation of BPA. The fetus and placenta have β -glucuronidase, which has the ability to deconjugate BPA. In rats, the placenta has high-levels of β -glucuronidase activity resulting in fetal exposure to deconjugated BPA. Also, although neonates conjugate BPA with sulfate using sulfotransferases, research on endogenous hormones has shown that biological activity does not end with sulfation. There is no reason to believe that BPA is completely de-activated by sulfation either. There are also local deconjugation reactions (Ginsberg and Rice 2009). Ginsberg's theories of deconjugation are not commonly held and are disputed by Vandenberg saying that this theory does not have enough scientific support (Vandenberg et al. 2007).

Health Effects of BPA

Health concerns from BPA exposure to humans are numerous. Several studies reflect concern over BPA's endocrine disrupting properties' ability to adversely affect reproductive development in both sexes. BPA exposure could be contributing to an increase in rates of heart disease, diabetes, obesity, brain development issues, altered behaviors, and reproductive cancers (Melzer et al. 2010; Vandenberg et al. 2007). In the occupational setting, where exposures can be much higher than in the general population, there is concern that BPA exposure can affect reproductive hormones (NTP 2008). BPA entered the mainstream spotlight in 2008 when Canada banned its use in baby bottles. The Canadian government was concerned with BPA leaching from infant formula cans, infant feeding bottles and drinking cups, and potentially having adverse health effects for infants (Environment Canada and Health Canada 2008a). BPA's possible estrogenic activity raised concerns since infants have a limited capacity to metabolize BPA and exposure to it is possibly associated with the early sexual development of children and some cancers. Only small changes in hormone activity during development can cause permanent effects (Welshons et al. 2003). There is also concern about prenatal maternal exposure possibly leading to reproductive and developmental issues for fetuses (Soto and Sonnenschein 2010).

Health Effects seen in Animal Studies

Numerous toxicological studies have been conducted to study the effects of BPA exposure on animals in an effort to understand human health effects. One of the earliest low-dose studies of BPA exposed pregnant mice to 2 and 20 µg/kg-BW/day. This fetal exposure to the male mouse resulted in an increased adult prostate weight relative to the

control males. This study was the first research to show that fetal exposure to BPA at the ppb level could alter adult reproductive systems in mice (Nagel et al. 1997). These early findings were confirmed by research that exposed pregnant mice to 50 µg/kg-BW/day of BPA. This fetal exposure caused the offspring to have increased prostate size, increased anogenital distance, and decreased epididymis weight. The androgen receptor binding activity of the prostate was also permanently increased (Gupta 2000).

The effect of BPA exposure during the perinatal period has been closely studied in animals. At this stage in development, the fetal and neonatal liver produces high levels of alpha fetoprotein (AFP). In rodents, AFP is the major estrogen binding plasma protein. This binding mechanism is believed to protect perinatal rodent tissues from overexposure to estradiol (Toran-Allerand 1984). BPA does not rapidly bind to AFP like estradiol, leaving it free to cause harm to sensitive tissues in the developing fetus or neonate. A region particularly susceptible to exogenous estrogens is the developing brain. When pregnant mice were exposed to BPA, sexual differentiation controlled by the brain was affected and the female offspring showed masculine behavior (Rubin et al. 2006).

Rodents exposed to BPA in adulthood have shown altered glucose homeostasis. After only a few consecutive days of BPA exposure, adult male mice experienced an elevation in pancreatic insulin levels, hyperinsulinemia, and insulin resistance. When pregnant female mice were exposed, they showed decreased glucose tolerance, and increased plasma insulin, triglycerides and leptin concentrations. Even after giving birth, these females retained their glucose intolerance, increased plasma insulin, leptin, and triglycerides, as well as experiencing an increase in their body weight (Alonso-Magdalena et al. 2006; Alonso-Magdalena et al. 2010).

Greater sensitivity to BPA has been shown in animal studies during the perinatal period. In a study where pregnant dams were given low doses of BPA in their water, alterations in their offspring's morphology and reproductive system were seen. Neonatal rats had an increase in body weight that was measurable soon after birth and continued into adulthood. The offspring also had altered estrous cycling and decreases of plasma luteinizing hormone. To see if these health effects could be seen if the BPA doses were applied to adult rats, the research team exposed post pubertal ovariectomized female rats with the same dose and a dose ten times higher. There were no uterotrophic responses in this test population, showing that the perinatal period had greater sensitivity. This study also showed the importance of investigating health effects from low-dose animal toxicology testing (Rubin et al. 2001).

The normal development of fat cells, or adipogenesis, has been shown to be disrupted by exposure to BPA. Increases in body weight have consistently reported in female rodents. Other increases in fat cell generation have been seen in offspring of pregnant dams exposed to BPA, as described above, rodents exposed in utero, and during lactation. Chronic exposure studies investigating body weight and adiposity throughout the rodent lifespan have not taken place (Howdeshell et al. 1999; Miyawaki et al. 2007; Rubin et al. 2001; Somm et al. 2009).

Animal studies have investigated BPA exposure and carcinogenesis, particularly breast cancer. In low dose experiments, rats prenatally exposed to BPA had increased incidence of changes in mammary gland structure and developing precancerous lesions during adulthood (Durando et al. 2007; Murray et al. 2007). When rats exposed

prenatally with BPA were then given an additional chemical challenge postnatally, they expressed greater susceptibility to carcinogenicity (Durando et al. 2007).

Reviews of animal toxicology of BPA literature differ in their conclusions depending on the inclusion criteria of the researchers. Harvard's Center for Risk Analysis (HCRA) performed a weight of the evidence evaluation focusing on male reproductive endpoints, in addition to other reproductive and development endpoints. They assessed 19 rat and mice studies and concluded that there is no consistent evidence proving low-dose effects in the endpoints they evaluated. This decision was founded on the uncertainty of the animal test results and the difference in the response pattern of BPA in comparison to other estrogenic compounds (Gray et al. 2004).

In a review directly following the HCRA evaluation, vom Saal and Hughes expressed concern at the use of only 19 animal studies in Gray's review. Their review included many more animal studies that were available for review in the HCRA study, but were not included. There were 115 *in vivo* studies regarding the low-dose effect of BPA. Ninety-four of these studies found significant effects. Of concern is that in 31 of the studies performed on vertebrates and invertebrate animals, health effects occurred at exposures below the EPA's reference dose of 50 µg/kg/day, a dose recognized as safe by the U.S. government (vom Saal and Hughes 2005).

Goodman's 2009 weight of evidence of animal studies included low-dose animal studies investigating developmental and reproductive endpoints published in peer-reviewed journals. Studies that administered BPA through oral exposure were given more weight since this is the route that humans are exposed and that which allows the first-pass detoxifying metabolism of BPA. Goodman's review, which agreed with earlier reviews

by Gray (Gray et al. 2004) and the author's own previous research (Goodman et al. 2006), concluded that the weight of evidence does not support the theory that low oral doses of BPA cause human reproductive and developmental harm (Goodman et al. 2009).

The Chapel Hill consensus statement, developed by a panel of experts from governmental and non-governmental institutions in 2007, expressed confidence that low dose BPA exposures to animals during the prenatal and neonatal time period “results in organizational changes in the prostate, breast, testis, mammary glands, body size, brain structure and chemistry, and behavior of laboratory animals.” In addition, this consensus statement is also confident that adult exposure of laboratory animals to BPA at low doses can cause neurobehavioral effects and reproductive effects in both sexes. This study also emphasizes that life stage can impact the pharmacokinetics of BPA (vom Saal et al. 2007).

The National Toxicology Program's (NTP) Center for the Evaluation of Risks to Human Reproduction convened a panel of experts in 2008 to review the reproductive and developmental risks of BPA. The twelve experts came from governmental and non-governmental institutions. Their risk assessment concluded that exposure to BPA raised “some concern for effects on the brain, behavior, and prostate gland in fetuses, infants, and children at current human exposures to bisphenol A.” NTP also expressed “minimal concern for effects on the mammary gland and an earlier age for puberty for females in fetuses, infants, and children at current human exposures to bisphenol A” (NTP 2008).

The Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) joined together and formed an expert panel in 2010 to review the literature on BPA. The meeting reviewed BPA in the food system and

consumer products. In reviewing animal toxicological data, the panel found BPA causing adverse effects in high dose studies evaluating traditional reproductive and developmental endpoints. When low-dose studies were investigated, it was discovered that this type of study often focused on new endpoints such as sex-specific neurodevelopmental, pre-neoplastic changes in mammary glands, and changes in prostates. For these endpoints, evidence of increased incidence would be concerning since these doses are similar to human exposure levels. Since these newer endpoint studies also investigate novel mechanisms of action, the panel found it premature to conclude that these animal data will translate to human health effects. They do recommend these studies to guide the direction of future research (FAO/WHO 2010).

Health Effects seen in Epidemiological Studies

In comparison to the abundance of animal studies, only a few human epidemiological studies have been conducted. Epidemiology studies on BPA have been criticized for having a limited weight of evidence due to their small samples size, cross-sectional design, limited details on subject selection criteria, and limited control for potential confounders (Vandenberg et al. 2007; Vandenberg et al. 2009). Although NHANES does use a cross-sectional design limiting ability to prove causality, its large representative sample can help provide information on trends worthy of further investigation. In an examination of the 2003-2004 cycle of NHANES data, an association was found between urinary BPA concentrations and cardiovascular disease diagnoses, diabetes, and abnormal liver enzyme levels (Lang et al. 2008). Combining the data from the 2003-2004 cycle with 2005-2006, research has shown an association with higher urinary BPA concentrations and higher reports of heart disease in adults (Melzer et al.

2010). In a subsample study of NHANES 2003-2008 data, a significant association was found between urinary BPA concentrations and the prevalence of obesity in children and adolescents (Trasande et al. 2012).

In a recent analysis, NHANES data was re-evaluated for associations between diabetes and coronary heart disease. This study, using what was defined as, “scientifically and clinically supportable exclusion criteria and outcome definitions,” did not consistently find any association with urinary BPA concentrations and heart disease or diabetes as previous studies have. An example of how their analysis differed from prior investigation is that this study utilized additional covariates in their regression models. For coronary heart disease evaluations, the researchers used the added covariates of heavy drinking, family history of heart attack or angina, hypertension, sedentary activity, cholesterol, and energy intake. They caution against use of NHANES to make any causal findings and encourage the use of different types of epidemiological studies to enable such findings (Lakind et al. 2012).

In a study investigating girls in early puberty and the environmental factors influencing their future risk to chronic diseases such as breast cancer, girls ages 6-9 years were recruited for a longitudinal study. In their pilot study work, researchers investigated the highest priority urinary exposure biomarkers. These included a panel of phytoestrogens, phthalate acids, and phenols. This study detected a wide variety of hormonally active exposure biomarkers, some at very high levels ($>1000 \mu\text{g/L}$). There were detectable levels of BPA in at least 94% of samples. The urinary BPA concentration varied by BMI, with girls with $<85^{\text{th}}$ percentile BMI having statistically significantly

higher urinary BPA concentrations than girls with BMI > 85th percentile (Wolff et al. 2007).

In an international study of BPA, a cross-sectional study of Chinese adults was conducted. The participants' urinary BPA concentrations were compared to clinical and biochemical measurements. An association was found between an increase in urinary BPA concentrations and increases in rates of obesity and insulin resistance (Wang et al. 2012).

BPA Risk Characterization

Minimal research has been conducted to characterize the risk of BPA exposure of children. From Japan, a longitudinal study was conducted tracking urinary BPA concentrations of elementary school children. It followed nearly a hundred school children from 1st grade to 6th grade. BPA was detected in 100% of these children's urine in the first grade sample, 97% in the third grade, and 86% in the sixth grade. The concentration of urinary BPA also decreased over time. A possible reason for the decrease in urinary BPA concentrations was the reduction in the use of BPA in canned food in Japan. Another possible explanation for the decrease in urinary BPA concentrations is that the consumption of canned foods decreased. Also, the polycarbonate plastic serving dishes used in school cafeterias were replaced with polyethylene terephthalate (PET) during the time of the study (Yamano et al. 2008).

In a United States study based in North Carolina, nine pre-school children aged 2-5 years were studied in two daycare centers for aggregate exposure to pesticides and persistent organic pollutants, including BPA. During the 48 hour sampling period, indoor and outdoor air, floor dust, play area soil, and duplicate diet samples were collected at the daycare center and at the homes of participating children. Hand wipes and urine samples were also collected from each child. Time-activity diaries were completed to help correlate activities and exposures measured. This study concluded that the children's exposures were very low for most pollutants and that exposure levels were similar between the daycare center and home and between low- and middle-income households. As for BPA, the main environmental exposure was from indoor air. Overall, the primary route of exposure for BPA was from dietary ingestion (Wilson et al. 2003).

Wilson greatly expanded her exposure studies of BPA and other chemicals in young children to 257 preschoolers in 2006. Extensive environmental samples were taken in their homes and daycare for 48 hours. These included samples of food, beverages, indoor air, outdoor air, house dust, soil, swipes of participants' hands, and urine collection. BPA was measured in more than 50% of the samples of indoor air, hand wipes, solid food, and liquid food samples. It was estimated that highest potential aggregate dose, assuming 50% absorption, is 1.57 $\mu\text{g/kg-BW/day}$. This study concluded that BPA's main exposure is from dietary ingestion, accounting for 99% of exposure for children. The remaining 1% of BPA exposure is from inhalation (Wilson et al. 2007).

To study BPA metabolism and the effect of removing BPA from the diet, five families of four in the San Francisco Bay Area were closely monitored for eight days before, during, and after following a "BPA-free" diet. The basic structure of the study was that the families began urinary BPA monitoring while consuming their normal diets in the first two days of the study. Then, for the next three days, BPA exposures from the food supply were eliminated by supplying the families with catered meals carefully prepared with fresh, organic, whole foods without any plastic cookware and stored in glass containers. The participants were only allowed to supplement their supplied food with fresh foods and foods from glass jars. The families then returned to their normal diets and monitoring continued for two more days. Monitoring results show that urinary BPA concentrations declined by 66% during the intervention period of the study. Post-intervention, the urinary BPA concentrations returned to the pre-intervention levels. The researchers acknowledge that not all sources of BPA can easily be eliminated from the food system. If this were possible, then they should have seen a 99% reduction since

dietary BPA exposure is estimated to be 99%. One source of BPA exposure could be from milk that travels through PVC piping during processing. BPA has also been detected in whole eggs. The study also suggested that non-dietary exposures to BPA could be larger than previously estimated (Rudel et al. 2011).

In another BPA dietary study from the United States, study participants were assigned to eat canned soup or fresh soup using a randomized, single-blind, 2 x 2 crossover study design. They ate the type of soup they were assigned for lunch for five days. After a wash-out period of two days, the groups were switched and they ate the new type of soup for lunch for five days. Urine was collected on the fourth and fifth days of each study week. Consuming canned soup versus fresh soup increased the urinary BPA concentrations by 1221%. The urinary BPA concentrations of the participants after consuming canned soup were the highest measured in a non-occupational setting (Carwile et al. 2011).

Exposure assessment research from Japan investigated the relationship between source and exposure using two methods. The first method was to model aggregate exposure to BPA from inhalation and ingestion pathways using Monte Carlo simulation. The population was stratified into six age groups, including age appropriate BPA exposure sources such as toys, breast milk, formula, and baby bottles for infants. The dietary intake was based on information from the National Nutrition Survey in Japan that collects data for three consecutive days. The second method employed a backward calculation that used urinary BPA concentrations to estimate intake. This method also used Monte Carlo simulation techniques to account for uncertainty and variability of the model parameters. The average intake modeled in the aggregate exposure pathway model

for male adults in 1995 was 0.43 µg/kg-BW/day and for 2002 was 0.16 µg/kg-BW/day. In comparison, in the backwards calculation from urinary BPA concentrations, the averagely exposed adult male was estimated to have a much lower exposure of 0.028 – 0.049 µg/kg-BW/day. This study considered the backward calculation as more reliable since the relationship between urinary BPA concentrations and BPA ingestion has been verified in human experimental studies. Its limitations are that it cannot provide information about sources of food exposure and the urinary BPA concentration data only included adults (Miyamoto and Kotake 2006).

An aggregate risk assessment conducted in Switzerland studied the relative contributions of ingestion and inhalation exposure to BPA from a variety of sources. An aggregate exposure dose was calculated using ingestion and inhalation rates and known values of BPA contamination of food, house dust, air, and dental sealants from published literature. This research found that the main source of BPA exposure for infants and children is from PC baby bottles and for adults is from canned food (von Goetz et al. 2010).

Food Contact Materials Regulations

In the United States, food contact materials regulations originated with the Federal Food, Drug and Cosmetic Act of 1958, section on Food Additives (21USC348). All substances used as food additives not already approved for use before September 8, 1958 were subject to authorization under this act. There is no restriction on the quantity of an approved substance that can be present in a product, just a regulation on how much exposure could result from food contact with the substance. For a new substance to get approved, it must undergo testing and show that it will not exceed certain consumer exposure levels to food packaging contaminants. The consumer exposure levels are called the cumulative estimated daily intake, or CEDI. CEDI's are determined by leaching experiments into food simulants or through modeling (Muncke 2009). The CEDI calculations are based on consumption factors, the percentage of a person's diet predicted to come in contact with a specific food-contact material, and food distribution factors, the percentage of all food contacting each material that is aqueous, acidic, alcoholic, or fatty (Duffy et al. 2006).

If a compound is approved as an additive to food packaging by the Food and Drug Administration (FDA), it must comply with different requirements depending on its CEDI. The CEDI requirements fall into three categories. A Threshold of Regulation (TOR) applies to substances with CEDI's of 1.5 µg/person/day or below and if the substance does not demonstrate carcinogenicity or structural similarity to any compound with carcinogenicity. No experimental toxicological data is required if a substance falls into this category. To qualify for a Food Contact Notification (FCN), a substance needs to have a CEDI below 3 mg/person/day. This method is the most expedient pathway for

authorization, but this approval only allows usage to the applying company. For substances with an estimated CEDI greater than or equal to 3 mg/person/day, an Indirect Food Additive Petition is required. The final category of authorization for food contact materials are for substances Generally Regarded as Safe, or GRAS (Muncke 2011).

In the United States, current food contact material regulations only require reproductive toxicity testing for intentionally added substances that might leach into food simulants at 1 ppm, or 1 mg/kg food or higher. This standard is 5 ppm or higher in the European Union (EU). Translated into an exposure dose, for an adult who is 60 kg and consumed 3 kg of food and liquids per day, an exposure up to 50 µg/kg BW/day could occur without requiring reproductive toxicity (Muncke 2011).

Current food contact materials regulations focus on mutagenicity and genotoxicity testing. This narrow scope fails to examine endocrine disruption, the toxicity of mixtures, and developmental toxicity. If these approaches were incorporated into current toxicological regulatory frameworks, there would be greater protection to women of childbearing age and pregnant women who are more sensitive to these types of exposures. Another vulnerable population are overweight and obese persons whose bodies' ability to metabolize xenobiotics have been altered (Muncke 2011).

In the European Union, the Framework Regulation 1935/2004 outlines the requirements for food packaging and its Article 3 pertains to food contact materials. The EU food contact materials regulations are based on substance migration from the packaging to the food simulants. The general plastic packaging leaching limits are regulated by the Plastics Food Contact Material Directive. Individual substances authorized for use are governed by specific migration limits (SML). SML's are based on

Tolerable Daily Intakes (TDI), so if a substance does not have a TDI, then there will not be an SML. BPA has an SML of 0.6 mg per kg of food in the EU. For starting substances such as monomers or other compounds that initially react to form a monomer are put on a “positive list”. Substances that are considered non-intentionally added substances (NIAS) do not need specific authorization. NIAS are impurities added to the polymer chemistry in the manufacturing of plastic materials and side products of the polymerization process. There are tiers to the required types of toxicological testing based on potential migration. The EU regulations take special exception to packaging that have a functional barrier between it and the food. These compounds do not need to be authorized for use in food packaging. The Fat Reduction Factor (FRF) is applied to foods that contain more than 20% fat. Even though more lipophilic packaging compounds would migrate into the food, the government regulation assumption is that consumption is low. Essentially, there can be higher migration for these fatty substances because an FRF is applied to calculate this food’s migration value (Muncke 2009).

There is concern that current food contact materials regulations may underestimate risk because migration testing with food simulants instead of with actual food may not represent real world exposures. Since more than 50 endocrine disrupting chemicals are approved for use in US and EU, (Muncke 2009) it is essential that the regulatory required toxicology testing reflects what is needed to accurately assess risk of food contact with endocrine disrupting chemicals.

Bisphenol-A Regulations

Although the safety of BPA used in food packaging has been debated in the scientific community since the 1990's, BPA moved into the mainstream spotlight in 2008 when Canada banned its use in baby bottles. Canada, the first country to ban the use of BPA in baby bottles, based its decision on scientific research indicating newborns and infants were at greatest risk for adverse health outcomes from BPA exposure. Many countries quickly followed suit in proposing bans of BPA, with success in Turkey, France, Sweden, and Denmark. In 2011, bans of BPA in China and Malaysia were enacted. The United States government was much slower to act in removing BPA from infant feeding systems, rejecting legislative efforts to ban BPA for years. BPA's use regulations and bans for the United States, the European Union, Canada, and Japan are detailed as following.

Bisphenol-A: United States

Bisphenol-A, which may leach or migrate into food from its packaging, is regulated by the Food and Drug Administration (FDA). 21 CFR §177.1580 regulates polycarbonate (PC) polymers, such as what are used in water and infant bottles. 21 CFR §175.300 (b) (3) (viii), 21 CFR §177.1440 and 21 CFR §177.2280 regulate BPA containing epoxy-based enamels and coatings used as inner linings for canned foods (FDA 2009). BPA has been approved for use in food packaging under food additive regulations since the 1960's. There is no specific migration limit for BPA or a restriction in the amount of BPA that can be in a final product. Current regulations for new packaging materials being added to the marketplace are more stringent, but since BPA has already been approved for use, any manufacturer can start using BPA without

notifying the FDA. They also do not need to disclose any information about their formulations. Manufacturer's submittal of a food contact notification for their current uses of BPA is voluntary (FDA 2012c).

In a report from one of its food safety laboratories, FDA acknowledges that BPA migrates into food from its packaging. It states "suspected endocrine disruptors are present as additives or residues in food-contact materials" and "can be expected to migrate to some foods in very low amounts. Larger amounts of migration can be expected from polymers exposed to food at elevated temperatures, i.e., heat-processed foods." Due to this known migration of chemicals and elements from food packaging, it is being monitored in the United States by FDA laboratories. Research from these labs have shown the presence of endocrine disruptors in cheese, infant formula, PC water carboys, canned food, apple juice, and plastic film food wrapping such as Saran wrap (McNeal et al. 2000).

According to the CDC, BPA is not considered mutagenic and is classified as unlikely to be a carcinogen (CDC 2009). The Environmental Protection Agency (EPA) does not classify BPA as bioaccumulative, persistent, or a toxin (EPA 2012a). Bisphenol-A's Oral Reference Dose (RfD) has been established by the US EPA since 1993 as 50 $\mu\text{g}/\text{kg}/\text{day}$. A reference dose is defined as a dose that can be ingested daily throughout a lifetime without any increased risk of adverse health outcomes. The BPA reference dose is based on the critical effect of reduced mean body weight in rats. The RfD is calculated from the lowest observed adverse effect level (LOAEL) of 50 $\text{mg}/\text{kg}\text{-day}$ since a no observed adverse effect level (NOAEL) was not observed. The research discovering this LOAEL was conducted in 1988. A safety factor of 1000, which is composed of a factor

of 10 for human to animal studies, 10 for variability within the human population, and 10 for the extrapolations from subchronic to chronic exposures, is applied to the LOAEL to calculate the RfD (US EPA IRIS 2012). The importance of the RfD is that risk assessments evaluating the safety of BPA exposures are based on this number, considering exposures lower than the RfD to be of low concern. There is debate about the legitimacy and relevance of using this RfD since it is based on a handful of high dose toxicity studies performed by private, industry-funded laboratories. These industry laboratories followed Good Laboratory Practices (GLP), criteria that were instated for private laboratories used for governmental research. The GLP movement resulted after an expansive two-year investigation of poor, and sometimes criminal, private research practices. Nonetheless, the industry data are still being used as the basis for establishing the reference dose even though subsequent studies have shown low dose effects of BPA (Myers et al. 2009).

In September 2008, the Natural Resources Defense Council (NRDC), an advocacy group, petitioned the FDA to prohibit the use of BPA in human food and packaging and to remove any approvals that allow BPA to be an additive in food. When the government did not answer the petition in the allowable timeframe, the NRDC decided to file a lawsuit against the agency. The FDA's answer finally came on March 30, 2012. At that time, the agency denied the petition based on insufficient scientific evidence warranting a ban (FDA 2012a). FDA's current stand on BPA, as expressed on their web-site, states that there is "some concern about the potential effects of BPA on the brain, behavior, and prostate gland of fetuses, infants, and children." It conveyed reluctance to take a firmer stand on BPA because the agency's review of the weight of

evidence did not demonstrate consistent and conclusive data about the negative impact of BPA (FDA 2012c).

Although legislative efforts at the federal level have faltered, many efforts at the city level, county level, and state level have been successful. The City of San Francisco was the first to recognize the risk of BPA exposure to infants and children, passing an ordinance banning toys and child care items containing BPA from being sold in June 2006. This ordinance was never enforced and was repealed in May 2007. Chicago was the first major city to ban the sale of baby bottles and sippy cups with BPA, Suffolk County of New York the first county to pass a similar BPA ban, and Minnesota and Connecticut, the first states to ban the use of BPA in infant feeding systems. Eleven states and the District of Columbia had passed legislation restricting the use of BPA for food contact applications by the time the federal government banned the use of BPA for baby bottles and sippy cups (Consumers Union 2009; National Conference of State Legislatures 2013; San Francisco Health Code 2007).

An integral driving force for change in BPA use in the U.S. has been consumer demand. When their products were cleared from major retailer shelves, companies took notice and began to remove BPA from consumer products such as PC baby bottles, sippy cups, and re-usable water bottles such as those produced by Nalgene. The rapid removal of BPA gave companies competitive advantage and prepared them for what seemed to be an inevitable ban on the use of BPA in their products. There was concern that health disparities could be created from the decision for major manufacturers to remove BPA from their infant feeding products. Advocacy groups have been vocal over concern that inequitable BPA exposures could be caused by the dumping of BPA containing infant

feeding products by large chain stores, like Wal-Mart, that have decided to remove these products from their shelves, onto discount and dollar stores (Breast Cancer Fund 2010).

In what was veiled as a change of opinion, the FDA amended BPA's use approval in the regulations, removing its ability to be used in polycarbonate plastic for infant feeding systems. The Federal Register posted on July 17, 2012, as an amendment to 21 CFR 177 the following:

“The Food and Drug Administration (FDA or the Agency) is amending the food additive regulations to no longer provide for the use of polycarbonate (PC) resins in infant feeding bottles (baby bottles) and spill proof cups, including their closures and lids, designed to help train babies and toddlers to drink from cups (sippy cups) because these uses have been abandoned. The action is in response to a petition filed by the American Chemistry Council (Federal Register 2012).”

It is important to observe of this amendment that the government acted in response to a petition from industry. To the uninitiated, this effort made the American Chemistry Council and the FDA look proactive. In actuality, this amendment was an effort to align the regulations with actions already adopted by manufacturers whose hands were forced to remove BPA by consumer demand. The amendment is very specific in only removing the use of PC resin from infant and toddler feeding systems. There is still no action regarding protection of other aspects of the food system that are marketed to infants and children, such as canned infant formula and canned baby food. There is also no protection of the food system accessed by adults. The American Chemistry Council should not receive any gratitude for petitioning the FDA. On the contrary, the American Chemistry Council has continually put intense pressure on any efforts to ban BPA from

packaging. Their lobbying has disrupted efforts to ban BPA from food packaging in several states. In California, the Toxin-Free Infants and Toddler Act law originally intended to protect the entire food system for infants and toddlers from BPA. In order for it to pass, legislators had to concede to not ban BPA in infant formula containers, even though this is the packaging where food spends the most time. The legislature was only able to pass a law banning BPA in baby bottles and sippy cups.

Bisphenol-A: Canada

Canada banned the use of BPA in baby bottles on April 18, 2008 after their risk assessment revealed that BPA is potentially harmful to human health and the environment. In an interview with the Washington Post, Canada's Minister of Health Tony Clement stated, "We have immediately taken action on bisphenol A because we believe it is our responsibility to ensure families, Canadians and our environment are not exposed to a potentially harmful chemical." Clement also stated that Canada's decision was based on a review of 150 worldwide studies. He added, "It's pretty clear that the highest risk is for newborns and young infants" (Layton and Lee 2008).

After this ban, a final screening assessment report for BPA was issued. This assessment was developed by the Canadian Environmental Protection Agency and Health Canada as part of a review of chemicals on the Domestic Substances List identified as potentially harmful to the environment or human health. The final assessment concluded that BPA meets the criteria for persistence but not bioaccumulation in the environment since it can only degrade under aerobic conditions. In evaluating the risk of biota in the environment, the report concluded that the biota could suffer long-term adverse effects at the current levels of exposure. The animal and human data show strong enough trends

towards reproductive and developmental harm to warrant the adoption of a precautionary approach to protecting human health (Environment Canada and Health Canada 2008a).

In the same year, Health Canada published a publicly available document outlining its BPA risk management approach. It finds there to be uncertainty in the conclusions about BPA's health effects from animal studies, but it believes there is enough evidence of adverse health effects that a precautionary approach should be applied to mitigate risk. They are using the ALARA, or As Low as Reasonably Achievable principle to minimize BPA exposure to newborns and infants from food packaging (Environment Canada and Health Canada 2008b).

Health Canada food research laboratories continue to monitor the food supply to ensure that the Canadian population's dietary exposure does not exceed the provisional tolerable daily intake (TDI) for Canada of 25 µg/kg BW/day. BPA exposure assessments of food and beverages are conducted by the Food Research Division. Their latest investigations included evaluations of BPA in canned food, canned liquid infant formula, bottled water, canned soft drinks, and baby foods in glass jars with metal lids. The BPA migration values from this research were used to model the Canadian population's estimated daily intake (Bureau of Chemical Safety 2010; Cao et al. 2010; Cao et al. 2010).

To strengthen their ability to regulate BPA, Canada added BPA to its list of toxic substances in October 2010.

“A scientific assessment of the impact of human and environmental exposure to bisphenol A has determined that this substance constitutes or may constitute a

danger to human health and the environment as per the criteria set out under section 64 of the Canadian Environmental Protection Act, 1999 (CEPA 1999, also referred to as “the Act”)... This addition enables the Minister to develop a proposed regulation or instrument to manage human health and environmental risk posed by this substance under CEPA 1999. The Ministers may also choose to develop non-regulatory instruments to manage these risks” (Canada Gazette Part II 2010).

Bisphenol A: European Union

In 2002, the European Commission Scientific Committee on Food assigned BPA a temporary tolerable daily intake (TDI) of 0.01 mg/kg BW day. TDI's are set at a level where this dose can be ingested on a daily basis over a lifetime safely, even for infants and children. This TDI was based on a three-generation dietary rat study that included reproductive and endocrine-related endpoints. In this study, a NOAEL of 5 mg/kg-BW/day was established with an uncertainty factor of 500 (EFSA 2006; EFSA 2010; EFSA 2012a; Thomson and Grounds 2005). The specific migration limit of 0.6 mg/kg for the European Union (EU) is based on the TDI (Muncke 2009).

In 2006, the European Food Safety Authority (EFSA), the EU's equivalent to the FDA, published an “Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids, and Materials in Contact with Food on a request from the Commission related to BPA.” This report concludes that “low-dose effects of BPA in rodents have not been demonstrated in a robust and reproducible way.” The agency believes that there are such differences in the toxicokinetics between rodents and humans that there needs to be caution in interpreting the results of rodent studies, especially ones showing adverse

effects from low doses. The report additionally discusses how it believes that the rapid metabolism of BPA in humans and primates results in low bioavailability and reduces the need for concern for overexposure. Rodents may have greater exposure because of the need for the metabolized BPA to go through the kidneys before excretion, allowing for further exposure. The robustness of studies is questioned, including how effects were measured, the number of doses investigated, the numbers of animals in the study, and the comparability of the low-dose studies to other traditional studies (EFSA 2006).

In this report, EFSA has set the TDI of 0.05 mg/kg-BW/day based on its risk assessment. The 0.05 mg/kg-BW/day has a 100 fold uncertainty factor applied to the NOAEL of 5 mg/kg-BW/day. With the review of new data, the EFSA reduced the uncertainty factor from 500 to 100. The uncertainty factor of 500, used to derive the temporary TDI, no longer needed the factor of five for uncertainties in the database on reproductive and developmental toxicity based on new scientific studies. This report estimates the population's estimated daily dietary exposure to BPA based on migration values. The estimated exposure from food for all population groups was less than 30% of TDI. These estimated doses are from exposure to BPA from its migration into the food from storage. It does not account for exposure to BPA from microwaving the food in a plastic container, BPA from PVC drinking water delivery pipes, or other non-dietary exposure pathways (EFSA 2006).

The EFSA issued another scientific opinion in 2008. In this report, the agency reviewed the BPA metabolic differences between infants and adults. The review confirmed that BPA exposure is modeled to be well below the TDI. In addition, it

sustained its belief that rapid metabolism will protect the body from BPA overexposure (EFSA 2012a).

The EFSA's scientific opinion of 2010 described how the agency EFSA reviewed more data on BPA in three areas. The first were animal data on neurodevelopmental effects performed by Stump in 2009. Secondly, the agency reviewed the literature published between 2007 and July 2010 that focused on toxicokinetics and human and animal toxicity. Third, they reviewed the risk assessment data supporting the Danish ban on BPA for food contact materials for infants 0-3 years old. They concluded that there was not sufficient evidence to necessitate changes to the current TDI (EFSA 2010).

In early 2011, the EU passed legislation to ban BPA from the manufacturing of polycarbonate infant feeding bottles starting in May 2011. The legislation also prohibited the marketing and importation of baby bottles with BPA components into the European Union starting in June 2011 (European Union 2011).

In September 2011, the French Agency for Food, Environmental Occupational Health and Safety, called ANSES, released a report that stated the agency's belief that BPA has an impact on human health. Since this ANSES report expressed different conclusions than EFSA, EFSA reviewed the report to see if there was a need to alter their scientific opinion on this subject. After investigation, EFSA did not believe it to be necessary to alter its opinion on BPA. The ANSES report came to different conclusions because it was structured differently than EFSA's research. It was a hazard identification that included non-food exposures, and the EFSA review was a full dietary risk assessment (EFSA 2011).

As a result of the ANSES report on BPA, France made a decision that was in contrast to the opinion of most EU country's governments; its National Assembly passed a law in October 2011 to ban BPA from all packaging in February 2012. This law will be phased in, first banning the use of BPA in products marketed to children less than three, and then banning BPA in all food containers by January 2014 (EFSA 2011). The target phase out date has since been pushed out to 2015.

The latest information from the EFSA was issued in the beginning of 2012. EFSA's Food Contact Materials, Enzymes, Flavourings and Processing Aids, or CEF panel, decided to start a complete re-evaluation of the human risks of BPA to humans from dietary and non-dietary sources to get a complete exposure profile. It is also considering low-dose rodent studies in its evaluations for human health. A report from this investigation and the associated meetings has not yet been released to the public (EFSA 2012b).

Feasibility of Removing BPA Out of the Food System

Logically, the simplest way to remove BPA from the food system would be to eliminate the use of BPA monomers for the production of polycarbonate plastics and the manufacture of the epoxy resins used in can linings. As more research is conducted on hormonal activity of plastics, it is being discovered that polycarbonate plastics and epoxy resins are not the only plastic polymers with estrogenic activity. BPA and other estrogenic compounds can be created unintentionally in plastic manufacturing. Some research has shown that the BPA-free plastic containers currently on the market express estrogen activity (Yang et al. 2011). In addition, even if regulations did demand that BPA be removed from all can linings, the challenge still remains to find alternative materials that can perform as well as BPA containing epoxy resin.

In a thorough review of the estrogenic activity (EA) of plastics used in the food system, lab analysis was conducted on 455 plastic products purchased in the supermarket. Estrogenic activity was found in almost all of these products, even those that were advertised as BPA-free. This research came to two conclusions. One, diagnostic tests that only use one kind of solvent will likely mischaracterize a substance as being EA-free. They recommend the use of both a more-polar and less-polar solvent for testing. Secondly, they believe that common stress testing, such as microwaving, heating, and UV exposure will allow for more accurate diagnosis of estrogen activity. Yang's research team tested alternative plastic materials to identify estrogen activity-free materials. They identified clarified polypropylene as being a polymer that is EA-free and can be purchased at an equivalent cost as current materials in use (Yang et al. 2011).

As for alternatives to the epoxy resin can linings, some food companies have already changed their packaging to reduce or eliminate the consumer's exposure to BPA. One such company is Eden Foods, whose cans and jars are all produced by the Ball Corporation. For a year and half the company tried to find out which chemicals were used in the manufacture of the cans they were using in their canned goods. They discovered that can manufacturers are protected by trade secret rights and did not need to disclose their products' chemical composition. The only company who would engage Eden in a dialogue was the Ball Corporation. Although they never disclosed which chemicals were used in their manufacturing process, they informed Eden Foods of an older can coating technology, oleoresin enamels. Oleoresin is made from a mixture of oil and resin derived from pine or balsam fir trees and is naturally BPA free. Now Eden Foods uses Ball produced oleoresin cans for all of their low acid bean products at an increased cost (Eden Foods 2013).

Can manufacturers continue to evaluate alternative coatings and report that there is no suitable material for high-acid products. For their high acid food such as tomatoes, Eden Foods uses jars with special, dually coated lids. The first coating on the metal lid contains BPA. The second layer, the one that is in contact with the food, is a BPA-free coating (Eden Foods 2013).

The packaging industry, as a whole, is not moving to alternative can linings. They are reluctant to transition back to oleoresin technology, one that was developed in the 1940's, seeing it as outdated and inferior to current technologies. Industry continues to research alternative chemistries, possibly to prepare themselves for imminent legislative mandates. They report a significant challenge in finding products that can meet all of the

performance and safety specifications needed for food and beverage containers. It also takes years to develop, test, and then get FDA approval for new technologies (Packaging Digest 2012a). Can manufacturers also need to consider developing alternative linings that can be used by multiple food manufacturers, can be produced at a competitive cost, and have minimal environmental and health impact (Lakind 2013).

Readily available alternatives to plastics and epoxy lined cans are glass, stainless steel, and aseptic packaging. Some of these alternative products are already in the marketplace in select product lines in the United States and more commonly used in other countries. A type of aseptic packaging now used for soups, stocks, and other liquids are Tetra Paks and SIG Combibloc. Some alternative plastic packagings are polyethylene terephthalate (PET) to replace PC plastic, metallocene polypropylene (PP), high-density polyethylene (HDPE), polyamide (nylon) or some co-polyesters. Besides oleoresins, the packaging industry suggested using polyester and polyacrylate can coatings, alkyd resins, and polyvinyl chloride (PVC) organosols as alternative metal can linings. Research on BPA migration from organosol lined cans (Munguia-Lopez and Soto-Valdez 2001; Munguia-Lopez et al. 2005) and from PVC products (Lopez-Cervantes and Paseiro-Losada 2003) have found estrogenic activity in these products, making them unsuitable alternatives.

Japan: Role Model in reducing BPA in the system

A strong public voice has driven consumer demand for companies to utilize alternative packaging methods to remove BPA from their products. Some countries, such as Japan, have made changes on a national level to remove BPA from products used or consumed by infants and children due to consumer demand. In its nationwide effort to

reduce BPA exposure from 1998-2003, the Japanese industry made significant changes even though it was not required by regulatory authorities. In its efforts to remove BPA from the food system, Japan replaced polycarbonate plastic food serving materials and substituted epoxy resin lining of cans with BPA-free polyethylene terephthalate (PET) (Miyamoto and Kotake 2006; Packaging Digest 2012b; Yamano et al. 2008). In a dietary exposure assessment, researchers tested for BPA in the new dishes used in a school cafeteria. They found no detectable BPA in the substituted dishes. Researchers were also able to detect a significant drop in urinary BPA concentrations in its study subjects from before and after the effort to remove BPA from the system (Yamano et al. 2008). Another effort of Japan to reduce BPA exposures was to remove BPA from thermal receipts in 2001. In a study of paper products, researchers confirmed that BPA is no longer detectable in Japanese thermal receipts (Liao and Kannan 2011).

Japan is a role model in protecting infants and children from potentially harmful food contaminants. Their actions reflect a precautionary approach led by consumer demand, as the Japanese government has not moved to regulate the use of BPA in food contact materials. These efforts acknowledge that children are particularly vulnerable to high BPA exposure levels. Research has shown that infants and children eat up to 10 times more food than adults do in comparison to their bodyweight. Additionally, children more frequently consume food from small packaging, leading to a larger surface-to-volume ratio of packaging to food and a higher migration of packaging chemicals per kg food (Muncke 2011).

Are the Current Regulations Protective Enough?

The common theme among governmental health agencies is that a BPA ban from the entire food system is not warranted because the general human population is not exposed to levels of BPA above the established RfDs and TDIs. Sensitive populations, such as infants and toddlers, are now protected by bans on the use of PC in baby bottles and sippy cups, the main source of this age group's exposure to BPA. They also express that there is no reason for concern about human health effects because humans are protected from adverse health effects of any BPA exposure by rapid metabolism. The animal experiments that show adverse health effects at levels below the RfDs and TDIs and at the same level as human environmental exposures continue to be discounted because the governmental reviews find flaws in how the experiments were conducted.

There are several reasons why it may not be appropriate to continue to regulate BPA exposure with the established RfD. RfDs are developed with traditional toxicology testing that applies the results of high-dose toxicity testing to a linear response curve to allow the extrapolation from one dose to another. A characteristic of endocrine disrupting chemicals is that they often display non-monotonic dose-response curves (NMDRC). This means that as dose increases, response cannot be expected to increase linearly. For NMDRC's, the dose response curve may begin with a high response, move to a low response at a moderate dose, and then have an increase to have a high response at the higher doses. This curve would appear as a U. Other times, a NMDRC could start out with a low response, have its highest response at moderate doses, and then show a decreased response again with higher doses. This curve would appear as an inverted U. Other times, curves could alternate between increasing and decreasing, forming a

multiphasic curve. With a NMDRC, one cannot predict the response from one dose knowing the response from a different dose (Vandenberg et al. 2012).

An additional reason why high dose exposures of rodent test animals may not be the best starting point for establishing exposure limits for EDC's is because high dose exposures may not reflect the real life, chronic, low-dose exposures experienced by humans. It is common for low-dose effects to be seen by endogenous and exogenous hormones (Vandenberg et al. 2012; Welshons et al. 2003).

Welshons' review discussed another aspect of why a linear dose response curve with a threshold may not be appropriate for regulating BPA. Welshons believes that the use of high dose toxicological studies for use with endocrine-disrupting chemicals with estrogenic activity (EEDC) will underestimate the bioactivity. Low dose biological activity can be predicted with knowledge of the hormonal action mechanism and the physiology of delivery of EEDCs. Linear extrapolations from high doses cannot predict the actions of EEDCs since this class of chemicals is receptor-mediated and receptors can saturate. As discussed by Vandenberg, EEDC's are known to display non-monotonic dose-response, where receptor-mediated response will first increase and then decrease as doses are increased. Dose-response relationships for EEDCs also need to recognize that endogenous hormones are already circulating in the system, therefore the system is already active, or above threshold, when exogenous hormones are applied in testing. The existence of endogenous hormones also indicates that there will be interaction with the exogenous hormones added to the system. This interaction needs to be accounted for in testing and risk assessment (Welshons et al. 2003).

An additional consideration supporting the need for current federal opinion of BPA health risks to be modified is the growing body of evidence that BPA does not solely act in the traditional estrogen receptor pathways. Studies have shown BPA to act in a variety of pathways, not just through the traditional estrogen receptors, to cause cellular response at very low concentrations. One newer mechanism of action of estrogenic compounds is with the membrane estrogen receptor (mER) from MCF7 estrogen target cells (Powell et al. 2001). Other research has shown that environmental estrogens such as BPA have binding affinity for the novel seven-transmembrane estrogen receptor GPR 30. After binding, alternative estrogen signaling pathways are activated (Thomas and Dong 2006).

Some scientists believe that BPA's rapid excretion in humans after first-pass metabolism is evidence that rat data showing effects at low doses is not relevant. Rats do not metabolize BPA in the same way as humans. In rats, BPA is excreted through the biliary/fecal pathway allowing enterohepatic circulation and the ability for deconjugation of BPA metabolites. The BPA can be released back into the system at this time (Ginsberg and Rice 2009). In response to arguments that rat studies should not be comparable to human studies because of their metabolic differences, Vandenberg's review reminds us that rat models of DES's potential effect on humans were accurate and foretelling (Vandenberg et al. 2009).

There is reason to call into question the validity of some of the animal studies in the BPA literature. One has to exercise caution in interpreting the results of any study, but especially one that was funded by industries that would suffer the most if adverse effects were found. The HCRA review found flaws in the studies they investigated,

stating the weight of the evidence for low dose effects is weak (Gray et al. 2004). This report was quickly disputed by vom Saal and Hughes, starting with the issue that only 19 studies were selected for review when many more have been published on the subject. In this review of the literature closely following the release of the HCRA report, 115 relevant studies were found that should have been evaluated. A great bias was found in the findings of these reports. Industry reports, such as the HCRA report funded by the American Plastics Council, have consistently not found any significant findings. On the other hand, >90% of government funded studies have found significant effects (vom Saal and Hughes 2005).

To understand the complexities of environmental estrogens in the human population, research needs to be conducted investigating the effect of mixtures of xenoestrogens. There is additionally a need to research the interaction of xenoestrogens and endogenous estrogens (Vandenberg et al. 2007). In cross-sectional research of the human population, there is an association with elevated levels of estrogens in the body and adverse health outcomes. The challenge with the current body of cross-sectional epidemiological research is that it cannot evaluate causality, determining whether the higher levels of this xenoestrogen result from the dysfunction or is the dysfunction caused by BPA.

In 2012, the EFSA and the EPA continued to push for more research and evaluations of endocrine disrupting chemicals in the food system. A new full evaluation addressing low-dose effects of endocrine disrupting chemicals and the validity of the current chemical testing methods is being conducted by EPA and partner agencies. The

report is due out by the end of 2013. These latest research endeavors show the potential for greater regulatory clarity in the near future.

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CHAPTER THREE

Manuscript 1

**An evaluation of urinary BPA concentrations and the consumption
of canned foods using NHANES 2003-2008**

Abstract

Objectives: The majority of Bisphenol A (BPA)'s ubiquitous exposure is from the food system where this chemical leaches from polycarbonate plastic food vessels and epoxy resin lined canned foods and beverages. BPA is rapidly metabolized in the body and can be readily measured in urine. This research investigates the dietary contributions that can be associated with the highest BPA concentrations by studying the diet of study subjects in the 24-hour exposure window prior to urinary BPA concentration testing. It seeks associations between urinary BPA concentrations and consumption of canned food and beverages accounting for demographic and socioeconomic factors.

Methods/Study Design: NHANES cycles 2003-2004, 2005-2006, 2007-2008 provide a nationally representative sample of 24-hour dietary recall information and urinary BPA concentrations for 7669 study participants. The associations between dietary contributions, urinary BPA concentrations, and the covariates of sex, age, race, education, income, creatinine, and serum cotinine are examined through statistical analysis including multiple linear regression modeling and factor analysis.

Results: Positive associations were found between urinary BPA concentrations and the number of canned foods, and specifically canned vegetables, canned pasta, canned beans, and canned soup consumed. The exploratory factor analysis revealed that the dietary patterns of the population with the highest BPA levels differed from that of the whole population and the population with the lowest BPA concentrations.

Conclusions: Findings of this study of three cycles of NHANES data continue to support prior BPA research that discovered that urinary BPA concentrations are highest in the younger populations, Non-Hispanic Black populations, lower income groups, lower

education levels, and smokers. Furthermore, this research identified specific canned food groups associated with higher levels of urinary BPA concentrations.

Background

Bisphenol-A (BPA) is a synthetic chemical with endocrine disrupting properties. In the 1930's, it was initially screened as a possible synthetic estrogen replacement (Cavalieri and Rogan 2010). Although BPA was not chosen for this application by the pharmaceutical industry, its usefulness as a building block for other consumer products was soon discovered. BPA is commonly utilized as a monomer base for polycarbonate plastic (PC). PC is widely used due to its properties of durability, shatter resistance, transparency, thermostability, and lightweight nature. BPA is also used as a linkage in epoxy resins. Epoxy resins, utilized in lining food and beverage containers, provide corrosion resistance, flexibility, and heat resistance. BPA is also used as a color developer in thermal receipts (Geens et al. 2012; Liao and Kannan 2011) and as a component of some dental composites (Joskow et al. 2006; Olea et al. 1996).

The use of polycarbonate plastics and epoxy resins in many consumer products has led to the annual manufacturing of BPA of over six billion pounds, making it one of the world's highest production volume chemicals (Melzer et al. 2010; Tsai 2006; Willhite et al. 2008). With so many contributing sources, BPA exposure in the human population is ubiquitous. BPA has been measured in the urine of 92.6 % of the American population (Calafat et al. 2008). Although BPA exposure has been detected in household dust and air (Wilson et al. 2007) and in water contaminated by landfill leachate (Vandenberg et al. 2007; vom Saal et al. 2007), diet is the main contributor of BPA exposure (Kang et al. 2006; von Goetz et al. 2010; Wilson et al. 2007).

BPA was first approved for use in food packaging in the 1960's (FDA 2012a). In the food system, BPA is found in polycarbonate plastic containers and in the epoxy resin

lining of canned food. This epoxy lining is found in traditional canned foods, as well as pre-prepared infant formula, on the lids of jars, and on the inside of aluminum beverage containers such as soda and beer cans. Polycarbonate plastics containing BPA are used to make plastic serving dishes, plastic serving utensils, and re-usable water bottles.

Although no longer approved for use in infant feeding systems since a July 2012 ruling by the FDA, at the time of the NHANES studies from 2003-2008 utilized in this research, BPA could be commonly found in PC baby bottles and sippy cups (FDA 2012b).

The concern of having BPA in food packaging is due to its propensity to leach into the product. It was first recognized to migrate from can linings into food by Brotons in 1995. Due to its incomplete polymerization in the manufacturing of epoxy resins, BPA molecules are free to migrate into the food (Brotons et al. 1995; McNeal et al. 2000). There have been subsequent studies showing that BPA can leach from polycarbonate plastic bottles, plastic storage containers, and PVC stretch film into food (Biles et al. 1997b; Brede et al. 2003; Lopez-Cervantes and Paseiro-Losada 2003; Yang et al. 2011).

When BPA is ingested by humans, it is biotransformed in the liver on its first pass into bisphenol A-glucuronide, a highly water soluble metabolite. BPA's half-life in the body is less than six hours. Evidence shows that BPA is completely cleared from the body in 24 hours (Tsukioka et al. 2004; Volkel et al. 2002). This rapid clearance from the body through urine makes total urinary species, comprised of free plus conjugated BPA, the most appropriate BPA exposure assessment marker (Melzer et al. 2010).

This research project focuses on the diet of study subjects in the 24-hour exposure window prior to urinary BPA concentration testing. The goal of this research project is to identify and analyze the dietary contributions that are known to be associated with the

highest bisphenol-A concentration levels in humans, canned food and beverages. Using regression modeling, this research will seek associations between urinary BPA concentrations and consumption of canned food and beverages, as identified by 24-hour dietary recall and accounting for demographic and socioeconomic factors. This study will additionally utilize factor analysis to identify dietary patterns of the participants, comparing the whole population with the subpopulations of participants with the highest urinary BPA concentrations and the lowest urinary BPA concentrations in order to identify eating patterns that could put people at risk for high BPA exposure.

Methods

Study population

This study utilizes three cycles of the National Health and Nutrition Examination Survey (NHANES): 2003-2004, 2005-2006, and 2007-2008. NHANES is a cross-sectional survey that employs a complex, multi-stage survey design. NHANES research is ongoing and the data are publicly available (CDC 2003; CDC 2005; CDC 2007a; CDC 2012a). These cycles of NHANES were chosen because the 2003-2004 NHANES cycle was the first nationally representative population based study of total BPA. Each subsequent survey cycle has followed the same BPA sampling plan. Urinary BPA concentrations, study variable URXBPH, were measured in a one-third subsample of the NHANES population as part of the Environmental Phenols panel. NHANES participants six years and older, male and female, were eligible to be selected for the environmental phenol subsampling. By cycle, the participants with no missing urinary BPA concentration data included in this study are 2003-2004: $n = 2517$, 2005-2006: $n = 2548$, and 2007-2008: $n = 2604$.

Biomonitoring measurements

Urinary samples for BPA concentration testing were taken when the NHANES participant visited the mobile examination center (MEC). All laboratory testing, blood, urine and swab testing, were conducted at the MEC. From the mobile van, the urine samples were frozen and sent to outside laboratories.

The processing laboratories used a lab method especially designed by NHANES to be sensitive to measuring BPA and other environmental phenols on the panel. Their

method utilized solid phase extraction (SPE) coupled on-line to HPLC and tandem mass spectrometry (MS/MS). They also used isotopically labeled internal standards to enable them to detect the lower levels of phenols in non-occupationally exposed persons, down to the detection limits of 0.1-2 nanograms per milliliter (ng/mL) for 100 μ L of urine (CDC 2007b). The detection limits within an NHANES cycle were consistent. For the 2003-2004 cycle, the lower limit of detection (LLOD) was 0.36 ng/ml. For 2005-2006 and 2007-2008, the lower limit of detection was 0.4 ng/ml. For analysis, all values below the limit of detection were based on the highest limit of detection across the three cycles, 0.4 ng/ml, with the formula of $LLOD/\sqrt{2}$, or 0.28 ng/ml (Barr et al. 2005; CDC 2007c; CDC 2009a; CDC 2011).

Dietary Measures

On the same day as the urinary BPA concentrations testing, the 24-hour dietary recall data is recorded by an interviewer during the Mobile Examination Center (MEC) appointment. This data is called “Day 1” since a second day of dietary recall information is recorded from a phone interview 3 – 10 days after the MEC appointment. With the established data that BPA is rapidly metabolized and is cleared in the urine in approximately 24 hours, this Day 1 24-hour dietary recall is an opportune data set to seek associations of BPA food exposure and urinary BPA concentrations (Stahlhut et al. 2009; Volkel et al. 2002; Volkel et al. 2005).

After the 24-hour dietary recall is recorded during an interview, the data are coded into food items using the USDA Food Codes. USDA Food Codes are adjusted with every two year NHANES cycle; removing codes that are underutilized and adding new codes for new commonly consumed food products. For this research project, in order to

conduct data analysis on BPA concentrations and their association with consumption of food potentially high in BPA, the USDA food codes were re-coded by NHANES cycle into 14 categories. The decisions on how to categorize the food codes were based on the supporting information provided by the USDA food code fields entitled “main description” and “additional description.” The food re-coding categories are: foods that are definitely canned as worded in their description, foods that are possibly canned, canned beverages, and foods that are not canned. Within the canned food codes, there was further categorization into nine canned food groups. The canned food groupings were based roughly upon categories utilized in published studies of BPA and canned food. These canned food groups were as follows: canned dairy, canned tomato, canned tuna, canned meat, canned fruit, canned vegetable, canned beans, canned soup, and canned pasta. For more details on which canned foods were placed in each food group, see **Appendix A**. Canned beverages were not readily recognized with food code descriptions. A method was devised to identify canned beverages using the USDA Food and Nutrient Database for Dietary Studies (FNDDS) food weights and food portion descriptions files (USDA 2006; USDA 2008; USDA 2010) merged with food code descriptions (Moshfegh A, personal communication).

Re-coding of the USDA Food Codes reaped the definitely canned food numbers of: 2003-2004: 265; 2005-2006: 257; 2007-2008: 258. Food codes that could possibly be canned were identified in these amounts by NHANES cycle: 2003-2004: 137, 2005-2006: 134, and for 2007-2008: 134. An example of a food code that is not definitively canned is 11631000. Its descriptions states, “High calorie beverage, canned or powdered,

reconstituted.” Since this food could be canned or powdered drink mix, it was placed into the “possibly canned” category.

Table 3.1: Canned Food Codes and Reported Consumption by Canned Food Category

Canned Food Group	Food Codes per Group NHANES 2003-2004	Food Codes per Group NHANES 2005-2006	Food Codes per Group NHANES 2007-2008	No. of canned items eaten	% of total canned food eaten
Dairy	13	12	12	262	6.7
Meat	29	28	28	1011	26
Tuna	3	3	3	116	3
Fruit	9	3	3	23	0.59
Tomato	8	8	8	38	0.97
Vegetable	143	143	144	1861	48
Beans	12	12	12	35	0.9
Soup	35	35	35	117	3
Pasta	10	10	10	431	11
total:	262	254	255	3899	100

Table 3.1 shows the number of food codes that were identified by the re-coding process per canned food category. It also displays the number of foods reported eaten per canned food category. Canned vegetables represent the majority of the canned food items that were identified, as well as the number of canned items that were consumed. The top three canned food groups eaten were canned vegetables, accounting for 48% of the canned food eaten, followed by meat, at 26%, and pasta, at 11%.

Re-coding of the USDA Food Codes was also necessary for the dietary pattern factor analysis. For this data reduction experiment, the food codes from the dietary recall data were split into 10 food groups. The food groups were milk, meat, eggs, legumes, grains, fruits, vegetables, fats, sweets, and beverages. The decision on food groupings was based on the broad food coding scheme outlined in the USDA FNDSS Documentation and User Guide (USDA 2006; USDA 2008; USDA 2010). In this study, the ninth FNDSS coding of “Sugar, Sweets, and Beverages” was split into the two

groups of sweets and beverages due to the significant consumption of beverages recorded by NHANES.

Statistical analysis

Statistical analyses of the NHANES datasets were performed with STATA. (STATA 11.2, College Station, Texas) Datasets were downloaded using the publicly available NHANES SAS XPT files imported into STATA. Statistical analysis used NHANES survey weighting for the BPA subsample adjusted for three survey cycles.

The urinary BPA concentrations were not normally distributed. The natural log was taken for the population to normalize, with the urinary BPA data represented in **Table 3.2** represented in geometric means.

After exploratory data analysis, the dataset was analyzed using simple and multiple linear regressions. The covariates selection for the multiple linear regression models were informed by previous NHANES and BPA exposure studies and were chosen a priori. They included gender, age, race, income, education, smoking, and creatinine variables. The age analysis utilized the variable accounting for age in years, RIDAGEYR, that were then grouped into five categories: 6-11 years, 12-19 years, 20-39 years, 40-59 years, and 60 years and up. These age categories allowed comparability of this research to other studies and a roughly even distribution of the population among the age groups.

The race covariate utilized the NHANES race categories as described in RIDRETH1. Many analyses of NHANES data re-code the race categories into the four groups of Non-Hispanic White, Non-Hispanic Black, Mexican Americans, and Other Hispanic/other ethnicity, Mixed Race, and then only report the first three. This study kept

all five race categories of Non-Hispanic White, Non-Hispanic Black, Mexican Americans, Other Hispanic, and Other ethnicity including Mixed Race in the analysis. Since this study combined three cycles, there were no issues with adequate sampling numbers for the two “Other” race categories. Power calculations were performed with an alpha of 0.05 and power of 0.8 to ensure that the numbers were adequate. As this study wanted to look at race as a factor in exposure to BPA, it was also important to preserve as much information about the race categories as possible for planning future public health interventions.

The education covariate used in this study was a composite of DMDEDUC2, which is the education variable for adults age 20 years and older, and DMDHREDU, which measures the education level of the head of household. This variable was applied for ages 6-19 years old to achieve comparability in education level measurements with the adult population.

The measure of income utilized for this study was the variable INDFMPIR which reports the poverty income ratio (PIR). Income category divisions were decided based upon the poverty income ratio cut points used for the public food assistance programs Supplemental Nutrition Assistance Program (SNAP) and the National School Lunch Program (NSLP). The income groupings were PIR 0.000-1.3000; 1.301 - 3.501, and 3.501 and above (CDC 1996). The highest reported PIR in NHANES is 5 (CDC 2009b).

The smoking covariate utilized the serum cotinine values from the variable LBXCOT to assess exposure to smoke from environmental exposures or active smoking. Serum cotinine is considered the best assessment tool for identifying smoke exposure over urine sampling for quantitative analysis. Testing for cotinine was available from 3

years old to 150 years. The cutoffs for smoking status were: serum cotinine of <LOD was considered not exposed, LOD – 10 µg/ml were passive smokers, and ≥ 10 µg/ml were considered as active smokers. Smoking could also increase a person's exposure to BPA since there is a transfer of BPA from thermal receipts during handling. This leads to dermal exposure and could lead to ingestion of BPA from hand-to-mouth movements during smoking behavior (Geens et al. 2012; Liao and Kannan 2011).

Urinary creatinine concentration, variable URXUCR, was included in the regression models since it has been shown to vary by age, sex, ethnicity, the time of day of urine sampling, and physical activity (Barr et al 2005). Creatinine measurements were taken for all participants with BPA measurements. Before the creatinine measurements were added into the regression model as an independent variable, the creatinine concentration was normalized by taking the square root. This is one recommended method to allow for BPA concentrations to be adjusted for urinary creatinine while still allowing the other covariates in the model to remain independent of urinary creatinine concentration fluctuations (Barr et al. 2005; Berko J, personal communication).

Exploratory factor analysis was employed as a data reduction method to analyze the dietary patterns of the study population. A factor analysis approach was indicated because out of the approximately 7000 USDA food codes, the population only reported eating 3954 different codes for all three cycles. At the tails of the BPA concentration population distribution, the number of codes reported greatly decreases. For the participants with the top 5 percent highest reported BPA concentrations, there are only 1282 food codes reported. A factor analysis can help identify the code families most highly consumed by the population (Kerver et al. 2003).

To choose the factors, a principal components analysis was utilized, along with principal components factoring and varimax rotation to assist in factor interpretation. Factor retention was based on eigenvalues >1.00 , scree plots, and parallel analysis. Variable retention was determined by factor loadings >0.4 and uniqueness of <0.5 .

After the factors were extracted, a sum scores by factors method was utilized to calculate factor scores for further analysis. Factor sum scores is a non-refined methodology that evenly weighted each reported serving in a food group (DiStefano et al. 2009).

Results

Table 3.2 details the population's average urinary BPA concentrations and average daily canned food and beverage consumption, stratified by gender, age, race, income, education, and smoking level.

Table 3.2: Demographics, BPA Concentrations, and Daily Canned Food and Beverage Consumption of NHANES 2003-2008

Variable	Categories	N (%)	GM ng/ml (CI) ¹	Average Daily Canned Food/Bev (CI)
Sample Population		7669	1.99 (1.89, 2.09)	0.39 (0.35, 0.43)
GENDER	Male	3793 (49.46)	2.14 (2.01, 2.27)	0.40 (0.36, 0.45)
	Female	3876 (50.54)	1.85 (1.72, 1.99)	0.37 (0.32, 0.44)
AGE	6 to 11	1059 (13.81)	2.65 (2.44, 2.88)	0.29 (0.20, 0.38)
	12 to 19	1818(23.71)	2.43 (2.24, 2.63)	0.33 (0.27,0.40)
	20 to 39	1695 (22.10)	2.29 (2.12, 2.47)	0.42 (0.36,0.47)
	40 to 59	1480 (19.3)	1.72 (1.58, 1.89)	0.43 (0.37, 0.49)
	60 +	1617 (21.08)	1.53 (1.42, 1.66)	0.36 (0.29, 0.43)
RACE	Non-Hispanic White	3190 (41.60)	1.90 (1.78, 2.02)	0.43 (0.38, 0.48)
	Non-Hispanic Black	1910 (24.91)	2.57 (2.39, 2.77)	0.36 (0.31, 0.40)
	Mexican- American	1781 (23.22)	2.08 (1.92, 2.26)	0.33 (0.26, 0.40)
	Other Hispanic	456 (5.95)	2.23 (1.85, 2.68)	0.23 (0.15, 0.31)
	Other Race/Multiracial	332 (4.33)	1.71 (1.36, 2.14)	0.20 (0.09, 0.31)
INCOME	PIR 0 - 1.300	2413(33.46)	2.38 (2.17, 2.61)	0.38 (0.33, 0.42)
	PIR 1.301 - 3.500	2773 (38.46)	2.01 (1.91, 2.25)	0.41 (0.34, 0.47)
	PIR 3.501 - 5	2025 (28.08)	1.74 (1.62, 1.87)	0.38 (0.32, 0.44)
EDUCATION	Less than high school	2257(29.95)	2.10 (1.91, 2.31)	0.38 (0.32, 0.45)
	High school grad	1845 (24.45)	2.02 (1.87, 2.19)	0.42 (0.36, 0.48)
	Some college	2077 (27.56)	2.15 (1.97, 2.35)	0.42 (0.36, 0.47)
	College grad +	1358 (18.02)	1.71 (1.55, 1.90)	0.33 (0.26, 0.40)
SMOKING	Not exposed	1320 (18.57)	1.64 (1.47, 1.83)	0.32 (0.26, 0.38)
	Environmental Exposure	4374 (61.54)	2.07 (1.95, 2.19)	0.40 (0.35, 0.46)
	Active Smoker	1414 (19.89)	2.04 (1.87, 2.23)	0.43 (0.36, 0.50)
BPA	Q1	1545 (20.15)	0.48 (0.46, 0.50)	0.13 (0.10, 0.16)
	Q2	1581 (20.62)	1.36 (1.34, 1.38)	0.09 (0.059, 0.13)
	Q3	1490 (19.43)	2.37 (2.34, 2.40)	0.14 (0.10, 0.18)
	Q4	1536 (20.03)	4.05 (3.99, 4.11)	0.14 (0.10, 0.17)
	Q5	1517 (19.78)	10.85 (10.11, 11.59)	0.19 (0.15, 0.23)

¹ GM= geometric mean, CI = 95% confidence interval

Key Results from Table 3.2

Gender: Male's urinary BPA concentration is statistically significantly higher than females, at 2.14 ng/ml with a 95% confidence interval (CI) of 2.01 and 2.27, as compared to 1.85 ng/ml (CI 1.72, 1.99) for females.

Age: When age is stratified, the youngest group, 6-11 year olds, has the highest mean urinary BPA concentration at 2.65 ng/ml (CI 2.44, 2.88). The urinary BPA concentrations decrease with each succeeding age group, with a statistically significant difference between the 20-39 year olds and the 40-59 year olds.

Race: Non-Hispanic Blacks' mean urinary BPA concentration is the highest amongst the race categories. Their geometric mean urinary BPA concentration is 2.57 ng/ml (CI 2.39, 2.77). The second highest BPA concentration is in the Other Hispanic group, with a concentration of 2.23 ng/ml (CI 1.85, 2.68), and the third highest is Mexican Americans with 2.08 ng/ml (CI 1.92, 2.26). Non-Hispanic Whites have the lowest GM BPA concentration of the three main racial groups.

Income: The population with the highest income level had the lowest concentration of BPA, which was statistically significant, with a mean urinary BPA concentration of 1.74 ng/ml (CI 1.62, 1.87). In contrast, the population with the lowest income has the highest BPA concentration of the income groups, with 2.38 ng/ml (CI 2.17, 2.61)

Education: The mean urinary BPA concentration is similar among the bottom three education groups. The highest education group, the population who have a college degree or higher or their head of household has a college degree or more for ages 6-19

years old, has the lowest BPA concentration. This concentration is statistically lower than the other groups, with a mean of 1.71 ng/ml (CI 1.55, 1.90).

Smoking: The majority of the population is passively exposed to smoke. Those that are not exposed to smoke have statistically significantly lower mean urinary BPA concentrations. Their BPA concentration is 1.64 ng/ml (CI 1.47, 1.83). Participants with passive and active exposure to smoking have higher BPA concentrations of 2.07 ng/ml (CI 1.95, 2.19) for passive smokers and 2.04 (CI 1.87, 2.23) for active smokers.

The last column of **Table 3.2** displays the average canned food and beverages consumed daily. As shown by the mean canned food and beverages consumed per day, males consume canned food more frequently than females, although this value is not statistically significant. The trend for canned food consumption by age is that consumption increases by age until the oldest group of sixty years or more. By race, non-Hispanic Whites consume more canned food and beverages than the other races. There is no trend to canned food and beverage consumption by income level, with the highest and the lowest income levels having similar lower values. Education strata displayed similar trends with the highest and lowest education levels having the lowest canned food and beverage consumption. The only statistically significant difference in canned food and beverage consumption was found for the smoking categories. The population with no exposure to smoking had the lowest reported values for consumption of canned food and beverages. Their mean exposure to canned foods was 0.32 servings (CI 0.26, 0.38) as compared to the passive and active smokers eating an average of 0.40 servings (CI 0.35, 0.46) and 0.43 servings (CI 0.36, 0.50), respectively. The use of the term “serving” in this

application relates to the number of eating events a participant reported for a certain food and does not correspond to a specific portion size.

Canned food analysis: As shown in **Table 3.3**, when the population's dietary recalls were coded into the canned food categories, 88% of the population did not report eating any canned food. Nearly ten percent reported eating one canned food item the previous day. Almost two percent had reported eating two or more canned foods. Many more people consumed food that was possibly canned, with 32% of the population reporting eating a food from this category. When canned food and beverage are both accounted for, nearly 25% of the population consumed one or more canned food items per day.

Table 3.3: Percent Canned Food and Beverage Reported

Canned Food/Bev Consumption	Canned Food %	Canned Beverage %	Possibly Canned Food %	Canned Food and Beverage %
No canned items	88.1	85.6	67.7	75.3
One canned item	9.9	10.7	23.6	18.1
Two or more	1.9	3.7	8.7	6.6

Key Results from Table 3.4

Results of the multiple linear regression models for 24-hour dietary recall data and urinary BPA concentrations are reported in **Table 3.4**. The models discovered a statistically significant increase in urinary BPA concentration with each reported consumption of canned foods for the whole population and for the adult population. With the whole population, with each one unit increase in canned food consumption, a 21%

increase in urinary BPA concentration is expected (CI 1.03, 1.32; p-value 0.00). For the adult population, a 20% increase in BPA concentration is expected for each one unit increase in canned food consumption (CI 1.09, 1.30; p-value 0.00). The models also show that a statistically significant increase in BPA concentrations can be expected for increased consumption of canned pasta, canned vegetables, canned beans, and canned soup for the whole population.

The consumption of possibly canned foods was statistically significant for the youth population, showing an increase of 17 % urinary BPA concentration with each one unit increase in consumption of possibly canned food. The youth models showed a significant increase of BPA concentration with each reported additional serving of canned pasta, tomato, beans, and tuna. The highest regression coefficient in the analysis is in the youth model, showing an increase of 14.7 ng/ml BPA for each additional serving of canned tomatoes. This is the only significant coefficient for tomatoes out of the three models. This large coefficient should be interpreted with caution since there was a limited ability to identify and code canned tomato products, there were very few reported tomato items being consumed. Due to this, a few instances of high BPA concentrations can impact the coefficient greatly.

In the adult population, a significant increase of urinary BPA concentration is expected with each unit of increased consumption of canned pasta, canned vegetable, canned beans, and canned soup. The highest coefficient is canned soup, with a 271% increase in BPA concentration expected with each reported instance of consuming this food. The regression models for the whole population display the same pattern as the adult population.

Table 3.4: MLR Regression Coefficients of NHANES 2003-2008 24-Hour Dietary Recall Data and Urinary BPA Concentrations

	<i>Youth Pop. (6-19 yrs)</i> (n=1816)		<i>Adult Pop. (20-83 yrs)</i> (n=3305)		<i>Whole Population</i> (n=5121)	
<i>Overall Food Categories:</i>	<i>GM ng/ml¹</i>	<i>p-value</i>	<i>GM ng/ml</i>	<i>p-value</i>	<i>GM ng/ml</i>	<i>p-value</i>
Canned Food	1.23 (0.98, 1.56)	0.08	1.20 (1.09, 1.33) 0.00		1.21 (1.11, 1.32) 0.00	
Canned Beverages	1.05 (0.92, 1.20)	0.44	0.99 (0.94, 1.05)	0.78	1.00 (0.95, 1.05)	0.99
Possibly Canned Food	1.17 (1.05, 1.30) 0.01		1.00 (0.93, 1.07)	0.99	1.03(0.97, 1.05)	0.34
Not Canned Food	0.99 (0.98, 1.00)	0.26	1.00 (0.99, 1.01)	0.40	1.00 (0.99, 1.01)	0.29
<i>Canned Food Sub-Cats.:²</i>						
Canned Dairy	0.93 (0.44, 2.00)	0.86	1.18 (0.56, 2.50)	0.66	1.12 (0.61, 2.03)	0.71
Canned Pasta	1.51 (1.22, 1.88)	0.00	1.80 (1.06, 3.08) 0.03		1.78 (1.19, 2.65) 0.01	
Canned Tomato	14.7 (11.79, 18.33)	0.00	0.74 (0.52, 1.05)	0.09	0.84 (0.41, 1.76)	0.64
Canned Vegetable	1.29 (0.93, 1.79)	0.11	1.30 (1.09, 1.53) 0.00		1.30 (1.11, 1.52) 0.00	
Canned Beans	1.57 (1.09, 2.25) 0.02		1.67 (1.10, 2.56) 0.02		1.67 (1.09, 2.56) 0.02	
Canned Tuna	0.76 (0.65, 0.89) 0.00		1.89 (0.82, 4.35)	0.13	1.48 (0.73, 3.00)	0.27
Canned Meat	1.16 (0.68, 1.99)	0.57	0.97 (0.78, 1.20)	0.76	0.98 (0.78, 1.24)	0.89
Canned Soup	1.43 (0.71, 2.87)	0.30	2.71 (1.19, 6.19) 0.02		2.30 (1.22, 4.34) 0.01	
Multiple linear regression models adjusted for gender, age, race, income, education, smoking, and creatinine						
¹ Geometric Mean (95% Confidence Interval)						
² Analysis conducted with canned fruit, not reported due to too few canned fruit food codes						

Factor Analysis Results

As displayed in **Table 3.5**, four dietary patterns emerged from factor analysis of the dietary recall data for the BPA subsample population for NHANES 2003-2008. The factors that emerged were loaded onto: factor 1- dairy, grain, and fruit (n=3, Cronbach's alpha=0.45), factor 2- meat and vegetable (n=2, alpha=0.36), factor 3- beverages and sweets (n=2, alpha=0.30), and factor 4- eggs, fats (n=2, alpha=0.21). These four factors explained 58% of the variance in the data.

In order to see if populations with highest and lowest biomarkers of BPA exposure has different dietary patterns than the population as a whole, separate factor analyses were performed for the lowest decile population, those with the lowest measured

urinary BPA concentrations, and the highest decile urinary BPA concentration populations. The population with the lowest decile displayed a similar dietary pattern as the whole population. It emerged with four factors with high factor loadings in similar groupings. Factor 1 for the lowest BPA population also displayed a dairy, grain, and fruit dietary pattern (n=3, alpha=0.44). Factor 2 was meat and vegetable (n=2, alpha=0.33). Factor 3 loaded highly with beverages and sweets (n=2, alpha=0.32), and factor 4, eggs (n=2, alpha=0.10). The percent of variance explained by these four factors was 63%.

The highest decile differed, with only three dietary patterns emerging. Factor 1 was loaded with meat and vegetable (n=2, alpha=0.44), factor 2- sweets, fats, eggs (n=3, alpha=0.30), and factor 3- fruit and grains (n=2, alpha=0.33). These three factors explained 53% of the variance in the data.

Table 3.5: Food Groups and Factor loadings for Dietary Patterns Identified in NHANES 2003-2008

Whole BPA Subsample Population (n=7314)		Population with lowest BPA (10%, n=739)		Population with highest BPA (90%, n=801)	
Food Groups	Factor Loading	Food Groups	Factor Loading	Food Groups	Factor Loading
Factor One: Dairy, Grain, Fruit		Factor 1: Dairy, Grain, Fruit		Factor 1: Meat, Vegetable	
Dairy ¹	0.72	Dairy	0.74	Meat	0.78
Grains	0.7	Grains	0.71	Vegetable	0.77
Fruit	0.54	Fruit	0.49		
Factor 2: Meat, Vegetable		Factor 2: Meat, Vegetable		Factor 2: Sweets, Fats, Eggs	
Meat	0.78	Meat	0.8	Sweets	0.73
Vegetable	0.75	Vegetable	0.77	Fats	0.7
				Eggs	0.44
Factor 3: Beverage, Sweets		Factor 3: Beverage, Sweets		Factor 3: Fruit, Grains, Beverage	
Beverages	0.75	Beverages	0.8	Fruit	0.82
Sweets	0.62	Sweets	0.58	Grains	0.56
				Beverages	-0.47
Factor 4: Eggs, Fats		Factor 4: Eggs			
Eggs	0.84	Eggs	0.87		
Fats	0.54				
¹ Food groups with factor loading > 0.4 retained					

The dairy, grain, fruit dietary pattern and the meat and vegetable dietary pattern were selected for further statistical analysis as these two dietary patterns accounted for 32% of the variance explained. **Table 3.6** displays the results of the factor sum scores method for the dairy, grain, fruit dietary pattern. When the factor sum scores were broken into quintiles, the percentiles show that persons following the dairy, grain, fruit dietary pattern are in the youngest age group, female, white, from a high income family, parents are well educated, and not exposed to smoking. As the association with the dairy, grain, fruit dietary pattern increased the mean urinary BPA concentration decreases.

Table 3.6: Factor Sum Scores by Quintile for the Dairy Grain Fruit Dietary Pattern

Dairy Grain Fruit Dietary Pattern							
Factor Sum Scores Quintiles:		Q1	Q2	Q3	Q4	Q5	P ¹
		%					
Age group	6-11 y	7	19	31	19	23	0.0000
	12-19 y	25	26	26	14	9	
	20-39 y	26	27	21	15	11	
	40-59 y	21	27	22	18	12	
	60+	10	25	26	19	20	
Sex	Male	21	26	24	15	13	0.0262
	Female	19	25	24	18	15	
Ethnicity	N.H. White	18	25	24	18	16	0.0000
	N.H. Black	31	29	22	11	6	
	Mexican Am.	17	26	27	17	13	
	Other	20	28	26	16	10	
Education	Less than H.S.	24	30	23	13	10	0.0000
	H.S. Graduate	24	26	24	14	12	
	Some college	21	27	24	16	12	
	College grad.+	12	21	23	23	21	
Income	0-1.3 PIR	27	28	22	12	10	0.0000
	1.301-3.5 PIR	20	26	25	16	13	
	3.501-5 PIR	16	24	23	20	17	
Smoking	Not exposed	9	20	26	25	20	0.0009
	Environ. Exp.	18	24	26	18	14	
	Smoker	31	33	17	12	7	
Mean BPA	in ng/ml	4.8	4.6	4.4	4	3.7	

¹ Wald's F Test

Table 3.7 displays the results of factor sum scores method for the meat and vegetable pattern. By examining the quintiles, this method displays shows that the person most likely to follow the meat and vegetable dietary pattern would be a young adult 20-39 years old, would be male, white, with a high income, well-educated, and a non-smoker. The mean BPA urinary concentration varies throughout the quintiles, not showing a consistent pattern of increasing or decreasing with loading on the meat and vegetable variables.

Table 3.7: Factor Sum Scores by Quintile for the Meat Vegetable Dietary Pattern

		Meat Vegetable Dietary Pattern					P
Factor Sum Scores Quintiles:		Q1	Q2	Q3	Q4	Q5	
		%					
Age group	6-11 y	40	18	16	17	9	0.0000
	12-19 y	40	18	14	18	10	
	20-39 y	28	15	12	21	24	
	40-59 y	27	13	16	22	22	
	60+	27	17	15	23	18	
Sex	Male	27	15	15	21	21	0.0013
	Female	32	16	14	21	17	
Ethnicity	N.H. White	29	15	14	21	20	0.8318
	N.H. Black	29	16	15	21	19	
	Mexican Am.	34	15	13	19	19	
	Other	32	16	15	20	18	
Education	Less than H.S.	36	17	15	19	13	0.0000
	H.S. Graduate	31	14	15	21	19	
	Some college	28	17	14	21	20	
	College grad.+	27	14	14	21	24	
Income	0-1.3 PIR	36	17	15	19	14	0.0002
	1.301-3.5 PIR	29	17	16	19	19	
	3.501-5 PIR	28	13	13	23	23	
Smoking	Not exposed	28	16	18	15	22	0.7736
	Environ. Exp.	28	15	14	23	19	
	Smoker	32	13	14	22	18	
Mean BPA	in ng/ml	4.6	4	4.4	4.3	4.5	

¹ Wald's F Test

In the bi-variate analyses between BPA concentrations and dietary patterns, there is a significant association between BPA and the dairy, grain, fruit eating pattern, as well as the sweets and beverage pattern and the fats and eggs pattern. The dairy, grain, fruit coefficient shows a 5% decline in BPA levels as the consumption of food in this dietary pattern increases (coefficient 0.95 ng/ml, CI 0.94, 0.97, p-value 0.00). For the sweets and beverage group, there is a 3% decline in BPA concentration as consumption of food in this dietary pattern increases (0.97 ng/ml, CI 0.96, 0.99, p-value 0.006). The fats and eggs dietary pattern followers have a similar trend, with a 5% decline in urinary BPA concentration with the increased consumption of fats and eggs (0.95 ng/ml, CI 0.92, 0.99, p-value 0.010).

Discussion

This study was successful in developing a method for identifying canned food and beverages from NHANES 24-hour dietary recall data using the USDA food codes and packaging information from the FNDDS files. When the canned food and beverage dietary information was paired with the participants' urinary BPA concentrations, associations confirmed the hypothesis that consumption of canned consumables is correlated with higher urinary BPA concentrations. This study was the first analysis of NHANES data for dietary contributions of BPA exposure using USDA food codes. Its strength was also to utilize this nationally representative sample to explore associations of exposure and biomarkers of dose.

One of the biggest challenges in this research was accurately identifying canned food from the dietary recall. The USDA food codes applied to the dietary recall are designed to capture the foods eaten for nutritional analysis. Their ability to be used for environmental health purposes is problematic because of the labeling of several similar food items with the same food code. The hardest group to capture in the canned food coding was canned fruit. For example, food code 63135110 is described as, "Peach, cooked or canned, not specified as to sweetened or unsweetened, not specified as to type of sweetener." The additional description is "peach, not specified as to raw, cooked, canned, frozen, or dried." In this case, this food code had to be placed in the "possibly canned food category." Peach in its different forms may be nutritionally equivalent, allowing an accurate nutritional analysis even when the different states are combined. For this environmental health analysis trying to find canned items, this combined grouping reduces the ability to use valuable data points. For this research, the most conservative

approach was utilized, only grouping foods into “canned food” if the food was definitively stated as being canned in the main and additional descriptions of the USDA Food Codes. This may have resulted in an underestimate of the canned foods consumed and weakened the associations between canned foods and urinary BPA concentrations.

Close inspection of **Table 3.1**, presented earlier, and the numbers of canned items per category identified by this methodology demonstrates the challenge in seeking reliable trends between BPA concentrations and canned food consumption. For example, the reported canned food consumed for canned fruit, tomatoes, and beans is each less than one percent of the total canned food consumed. According to USDA data, 6 % of all fruit available for consumption is canned (Buzby et al. 2010), making the finding of only 23 instances of canned fruit consumption out of 7669 people, or only 0.59% of canned food was canned fruit is likely an underestimate. The small quantities of food items identified in some food categories resulted in large standard errors for the regression coefficients in the regression modeling. The regression coefficients could not be calculated in STATA for the canned fruit variable due to the lack of data points.

Some food categories were more accurately identified by the canned coding methodology. Canned vegetables were identified by over 140 food codes, leading to the reporting of 1861 instances of canned food consumption for this population. This is a more precise reflection of the potential for canned vegetable consumption in the United States as the USDA has calculated that 24% of the total vegetables available for consumption are canned (Buzby et al. 2010).

Three canned food codes per NHANES cycle were not sorted into canned food sub-categories because the food properties were so different from the nine groups. These

three foods were sauerkraut, quail eggs, and coconut cream. They were included in the overall canned food category for analysis. Not including these three foods in the canned food categories had little impact on the results since quail eggs were not reported to being consumed in any of the NHANES cycles, and sauerkraut and coconut cream were only reported to be consumed by one participant for each food code for the 2005-2006 and 2007-2008 cycles.

Valuable information for research is contained in the USDA Food Codes Standard Reference (SR) links. These links describe the components of a food that were used to calculate nutritional analysis. For example, the food code 28340660 for “chicken or turkey vegetable soup, home recipe” is linked to 12 different SR items. These SR links often include canned food which would have been useful for this analysis. In this case, it is linked to “tomato juice, canned, with salt,” SR code number 11540. The recipes can only be used for nutritional analysis and do not necessarily reflect what people ate. SR codes for canned foods cannot be used for determining packaging. A preliminary study of SR links tested regression models that include the SR codes for canned foods into the analysis. No statistically significant associations were discovered, affirming the inability to use the SR codes for food packaging studies. The SR codes are rich with canned food links to USDA food codes: for 2003-2004, 1162 canned food codes; for 2005-2006- 1130; and for 2007-2008- 1312. To improve the dietary recall data’s ability to be used for environmental health food packaging studies, the SR Links may be a good starting point (USDA 2010).

A limitation of this study was to assess potential BPA exposure using only canned food and beverages. BPA is known to leach into food that is stored in polycarbonate

plastic food containers and from PVC stretch films. Foods can potentially be contaminated by BPA from other unknown sources. As packaging information was limited in the dietary recall data, the most definitive and well characterized categorization for BPA exposure, canned foods and beverages, was utilized for this analysis.

In this research study, an effort was made to stratify by racial categories whenever possible to enable this study to inform public health intervention for BPA exposure reduction in targeted populations. There are five racial categories coded in the NHANES data, with the fifth one being the race category of “other race, including multiracial”, a combination of Native Americans, Asian Americans, Pacific Islanders, and many other race and ethnic categories. Although at the time the survey is taken, more specific racial and ethnic data is collected, to allow for stronger analytical capabilities, the NHANES data is re-coded into five main racial categories. Even with this conglomeration, when the racial categories were stratified in this analysis, many strata were omitted due to lack of data points. It is challenging to build informed public health intervention strategies with data that may not represent the community where a public health scientist is working.

Factor analysis was brought into this environmental health study to examine how this data reduction method could be applied to an exposure assessment scenario. An additional reason for incorporating a factor analysis in this research was that the exploratory data analysis discovered that the participants with the highest BPA concentration did not have a significantly higher level of canned food and beverage consumption. Previous research has shown that canned food is the highest contributor to BPA exposure from the food system and food is the largest source of BPA exposure. Since, according to this data analysis, the population with the highest BPA concentrations

did not get exposed from canned food, the aim was for the factor analysis to help narrow down which foods could be contributing to the BPA exposures.

A success in the factor analysis was that the dietary patterns discovered are comparable to other dietary factor analysis studies. In Tseng's study, he discovered that there are two main patterns of food consumption in the United States. He coined them as the Western Diet, one that is based on British style cooking, and that of the American Healthy Diet, that is reflective of nutrition science's influences. This exploratory factor analysis discovered a similar Western Diet with the Meat and Vegetable factor as well as the American Health Diet identified by the Fruit, Grain, and Dairy factor (Kerver et al. 2003; Tseng 1999).

The factor analysis did not discover specific foods associated with high levels of BPA. Its analysis by BPA concentration deciles did show that the population with the highest BPA displayed a dietary pattern that differed from the dietary trends found in both the whole population and the population with the lowest BPA concentrations.

This factor analysis was exploratory in nature, discovering that the selection of only ten food groups for analysis limits the ability to narrow down exactly which foods could be causing the high BPA concentrations. Preliminary efforts in dietary factor analysis separated the dietary recall data into approximately 40 different food groups. This method has been successfully applied by other researchers to food frequency data representing dietary patterns for longer periods of time (Newby et al. 2004; Varraso et al. 2012). For these 24-hour dietary recall data, splitting the data into 40 categories lent to a high number of null values for food groups. These null values are especially problematic for factor analysis, forcing abandonment of this approach.

Conclusions

This exploration of NHANES dietary recall food codes as a means of identifying potential BPA exposure sources highlighted the need for improved collection of food packaging details in dietary studies to enable them to be used for environmental health applications. To better characterize BPA exposures in the United States and allow informed interventions and evaluation methods for reducing BPA and EDC exposures, a recommendation is to collect food packaging information during the dietary recall interviews and to retain all of the packaging information in the food coding. The current USDA food coding scheme utilized in the NHANES studies, often including fresh, canned and frozen produce into one food code, limited the ability to identify definitively canned food. The restricted identification of some canned food categories, for example, canned tomatoes and canned fruits, minimized statistical analysis capabilities. The highly detailed dietary packaging information will allow environmental health scientists the ability to assess dietary information on a nationally representative scale and seek associations between packaging exposures and health outcomes. Research of this magnitude has not taken place in the United States before.

Positive associations were found between urinary BPA concentrations and the number of canned foods, canned vegetables, canned pasta, canned beans, and canned soup consumed. When the population was broken into quintiles, the quintile with the highest BPA did not consume a significantly higher number of canned food and beverages. Their canned food and beverage consumption calculated by the survey was less than one serving, averaging only 0.19 servings. There are a couple of possible explanations for these findings in the data. The most plausible explanation for this result

is that the coding of the USDA food codes did not properly capture all of the canned foods consumed. An alternate explanation is that factors outside the food system are greater contributors to the urinary BPA concentrations in the NHANES population.

Youth population multivariable linear regression models were found to follow trends different from the whole population and the adult population. As with other studies of food packaging and environmental contaminants, this study may be confirming that due to their smaller body size, a similar dose will affect a child more than an adult. A contributing factor to the differential association found between canned food consumption and BPA concentrations is that children's food is often packaged differently than other food; with an emphasis on individual serving containers. The smaller packaging size leads to a larger surface area of the food being exposed to possible packaging chemical migration (Muncke 2011).

Factor analysis methods were applied to the dataset to further mine the dietary recall for indicators of specific food groups that could be contributing to high BPA concentrations. The exploratory factor analysis revealed that the dietary patterns of the population with the highest BPA levels differed from that of the whole population and the population with the lowest BPA concentrations. The dietary pattern differences in the highest decile give evidence that specific food groups could be contributing to higher BPA exposures. Future factor analysis studies of this dataset would benefit from bringing in the grams of food consumed to allow weighting of the factor sums. Additional analysis could also further divide the food groups, striking a balance among the 10 groups used in the final factor analysis of this research and the 40 food groups used in the preliminary research. Objectives of creating the food groups could be to single out the foods with

higher fat content and canned foods, two characteristics associated with food having a potential for higher BPA content.

Findings of this study of three cycles of NHANES data support prior BPA research that discovered that urinary BPA concentrations are highest in the younger populations, Non-Hispanic Black populations, lower income groups, lower education levels, and smokers (Braun et al. 2011; Calafat et al. 2008; Lakind and Naiman 2008). Populations that have reported low food security and have accessed emergency food assistance have also been identified as being vulnerable to higher BPA concentrations (Nelson et al. 2012).

A future research recommendation would be to collect dietary and biological data differently between morning MEC appointments and the afternoon and evening MEC appointments. For morning MEC appointments, the first urinary void on the day should be collected. These participants have been fasting for 9.5 hours, so this urinary sample would better capture the previous day's dietary exposure to BPA than the one collected at the morning appointment. Research has shown that it would likely be capturing the previous night's dinner exposure to BPA (Teeguarden et al. 2011). This extra step could be achieved by sending urine sample vials to the participants ahead of time. For afternoon and evening appointments, where participants have been fasting for 6 hours, dietary recall information should be collected about what they consumed earlier in the day. According to research from Teeguarden, the current spot-urine test collected in NHANES likely reflects the BPA exposure from the previous meal, or one that has occurred in the last 4-6 hours. It does not reflect the full day's exposure. Instead of trying to use the diet of the previous 24-hours to correlate with BPA, asking about breakfast exposures could be more

accurately associated with the urinary BPA concentrations collected in the MEC laboratory collections. The short time frame between consumption and dietary recall collection could improve the accuracy of the food consumption reported.

Although these suggestions contain additional tasks and would add cost for testing media, lab analysis, and interview time, these actions would enhance researchers' ability to characterize BPA dietary exposure. This expansion in the NHANES data collection could be an important step in strengthening epidemiologic data about BPA exposures. Epidemiologic data in this field is commonly criticized for having a small sample size limiting generalizability. NHANES is an opportunity to have a nationally representative sample to enable associations about exposure dose. This knowledge would improve the ability to plan dietary interventions, to guide food manufacturers on areas to reduce BPA use, provide data for BPA regulatory reform, and take more effective steps to protect the health of the public.

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APPENDIX A: Canned Food According to USDA Food Code Descriptions

Canned Food Category	Main Food Code Description	Food Code
DAIRY	INSTANT BREAKFAST, FLUID, CANNED	11611000
	PUDDING, CAN, CHOC, REDUCED FAT (INCL JELL-O LIGHT)	13220230
	PUDDING, CAN, CHOC, FAT FREE	13220235
	PUDDING, CANNED, NOT CHOC, REDUCED FAT	13220240
	PUDDING, CANNED, NOT CHOC, FAT FREE	13220245
	PUDDING, CANNED, NOT CHOCOLATE	13230110
	PUDDING,CANNED,LOW CAL,W/ARTIFICIAL SWTNR,NOT CHOC	13230120
	PUDDING, CANNED, CHOCOLATE	13230130
	PUDDING, CANNED, LO CAL, W/ ART SWTNER, CHOC	13230140
	PUDDING, CANNED, CHOC & NON-CHOC FLAVORS COMBINED	13230200
	PUDDING, CANNED, TAPIOCA	13230500
	PUDDING, CANNED, TAPIOCA, FAT FREE	13230510
MEAT	BEEF, ROAST, CANNED	21401400
	CORNED BEEF, CANNED, READY TO EAT	21416150
	HAM, SMOKED OR CURED, CANNED, NS AS TO FAT EATEN	22311500
	HAM, SMOKED OR CURED, CANNED, LEAN & FAT EATEN	22311510
	HAM, SMOKED OR CURED, CANNED, LEAN ONLY EATEN	22311520
	CHICKEN, CANNED, MEAT ONLY, LIGHT & DARK MEAT	24198570
	TURKEY, CANNED	24206000
	VIENNA SAUSAGE, CANNED	25221910
	VIENNA SAUSAGE, CHICKEN, CANNED	25221920
	HAM/PORK , LUNCHEON MEAT, CHOPPED, CAN (INCL SPAM)	25230530
	HAM, PORK & CHICKEN, LUNCHEON MEAT, CHOPPED, CANNED	25230540
	HAM, PORK & CHICKEN, LUNCHEON MEAT, CHOPPED, CAN, RED SODIUM	25230550
	FISH, NS AS TO TYPE, CANNED	26100180
	ANCHOVY, CANNED	26101180
	MACKEREL, CANNED	26121180
	SALMON, CANNED	26137180
	SARDINES, CANNED IN OIL	26139180
	SQUID, CANNED	26213190
	CLAMS, CANNED	26303180
	CRAB, CANNED	26305180

	LOBSTER, CANNED	26311180
	OYSTERS, CANNED	26315180
	SHRIMP, CANNED	26319180
	BEEF BROTH OR BOUILLON, CANNED, LOW SODIUM	28310120
	CHICKEN BROTH, CAN, LOW SODIUM	28340170
	GRAVY, POULTRY	28500000
	GRAVY, BEEF/MEAT (INCL GRAVY,NFS;BROWN GRAVY;SWISS STEAK GRV	28500040
	SPAGHETTI SAUCE W/ MEAT, CANNED, NO EXTRA MEAT	74404030
TUNA	TUNA, CANNED, NS AS TO OIL OR WATER PACK	26155110
	TUNA, CANNED, OIL PACK	26155180
	TUNA, CANNED, WATER PACK	26155190
TOMATOES	TOMATOES, COOKED, FROM CANNED, NS AS TO METHOD	74201003
	TOMATOES, FROM CANNED, STEWED	74204013
	TOMATOES, CANNED, LOW SODIUM	74204500
	TOMATO SOUP, CANNED, UNDILUTED	74602030
	TOMATO SOUP, CANNED, LOW SODIUM, READY-TO-SERVE	74602100
	TOMATO SOUP, CANNED, REDUCED SODIUM, PREP W/ WATER	74602200
	TOMATO SOUP, CANNED, REDUCED SODIUM, PREP W/ MILK	74602300
	GAZPACHO, CANNED, UNDILUTED	75604610
FRUIT	ORANGE SECTIONS, CANNED, JUICE PACK	61119020
	TANGERINE JUICE, CANNED	61213220
	GUAVA SHELL (ASSUME CANNED IN HEAVY SYRUP)	63125100
VEGETABLE	WHITE POTATO, CANNED, LOW SODIUM,NS AS TO ADDED FAT	71103200
	WHITE POTATO, CANNED, LOW SODIUM, NO FAT ADDED	71103210
	WHITE POTATO, CANNED, LOW SODIUM, FAT ADDED	71103220
	COLLARDS,COOKED,FROM CANNED,NS FAT ADDED	72107203
	COLLARDS,COOKED,FROM CANNED,FAT NOT ADDED	72107213
	COLLARDS,COOKED,FROM CANNED,FAT ADDED	72107223
	CRESS, COOKED, FROM CANNED, NS FAT ADDED	72110203
	CRESS, COOKED, FROM CANNED, FAT NOT ADDED	72110213
	CRESS, COOKED, FROM CANNED, FAT ADDED	72110223
	GREENS, COOKED, FROM CANNED, NS FAT ADDED	72118203
	GREENS, COOKED, FROM CANNED, FAT NOT ADDED	72118213
	GREENS, COOKED, FROM CANNED, FAT ADDED	72118223
	KALE,COOKED,FROM CANNED,NS FAT ADDED	72119203
	KALE,COOKED,FROM CANNED,FAT NOT ADDED	72119213

KALE, COOKED, FROM CANNED, FAT ADDED	72119223
MUSTARD GREENS, COOKED, FROM CANNED, NS FAT ADDED	72122203
MUSTARD GREENS, COOKED, FROM CANNED, FAT NOT ADDED	72122213
MUSTARD GREENS, COOKED, FROM CANNED, FAT ADDED	72122223
SPINACH, COOKED, FROM CANNED, NS FAT ADDED	72125203
SPINACH, COOKED, FROM CANNED, FAT NOT ADDED	72125213
SPINACH, COOKED, FROM CANNED, FAT ADDED	72125223
SPINACH, FROM CANNED, CREAMED	72125233
SPINACH, COOKED, FROM CANNED, W/ CHEESE SAUCE	72125253
TURNIP GREENS, COOKED, FROM CANNED, NS FAT ADDED	72128203
TURNIP GREENS, COOKED, FROM CANNED, FAT NOT ADDED	72128213
TURNIP GREENS, COOKED, FROM CANNED, FAT ADDED	72128223
TURNIP GREENS W/ ROOTS, CKD, FROM CAN, NS ADDED FAT	72128403
TURNIP GREENS W/ ROOTS, CKD, FROM CAN, NO FAT ADDED	72128413
TURNIP GREENS W/ ROOTS, CKD, FROM CAN, FAT ADDED	72128423
TURNIP GREENS, CANNED, LOW NA, NS AS TO ADDED FAT	72128500
TURNIP GREENS, CANNED, LOW SODIUM, FAT NOT ADDED	72128510
TURNIP GREENS, CANNED, LOW SODIUM, FAT ADDED	72128520
CARROTS, COOKED, FROM CANNED, NS FAT ADDED	73102203
CARROTS, COOKED, FROM CANNED, FAT NOT ADDED	73102213
CARROTS, COOKED, FROM CANNED, FAT ADDED	73102223
CARROTS, COOKED, FROM CANNED, CREAMED	73102233
CARROTS, COOKED, FROM CANNED, GLAZED	73102243
CARROTS, COOKED, FROM CANNED, W/ CHEESE SAUCE	73102253
CARROTS, CANNED, LOW SODIUM, NS AS TO ADDED FAT	73103000
CARROTS, CANNED, LOW SODIUM, NO FAT ADDED	73103010
CARROTS, CANNED, LOW SODIUM, FAT ADDED	73103020
PEAS & CARROTS, FROM CANNED, CREAMED	73111033
PEAS & CARROTS, COOKED, FROM CANNED, NS FAT ADDED	73111203
PEAS & CARROTS, COOKED, FROM CANNED, FAT NOT ADDED	73111213
PEAS & CARROTS, COOKED, FROM CANNED, FAT ADDED	73111223
PEAS & CARROTS, CANNED, LOW SODIUM, NS ADDED FAT	73111250
PEAS & CARROTS, CANNED, LOW SODIUM, FAT ADDED	73111260

PEAS & CARROTS, CANNED, LOW SODIUM, NO FAT ADDED	73111270
PUMPKIN, COOKED, FROM CANNED, NS AS TO ADDED FAT	73201003
PUMPKIN, COOKED, FROM CANNED, FAT NOT ADDED	73201013
PUMPKIN, COOKED, FROM CANNED, FAT ADDED	73201023
SWEETPOTATO, CANNED, NS AS TO SYRUP	73407000
SWEETPOTATO, CANNED, W/O SYRUP	73407010
SWEETPOTATO, CANNED IN SYRUP	73407020
SWEETPOTATO, CANNED IN SYRUP, W/ FAT ADDED	73407030
ARTICHOKE, GLOBE(FRENCH), CKD, FROM CAN, NS FAT ADDED	75201003
ARTICHOKE,GLOBE (FRENCH),CKD,FROM CAN,FAT NOT ADDED	75201013
ARTICHOKE, GLOBE (FRENCH), CKD, FROM CAN, FAT ADDED	75201023
ASPARAGUS, COOKED, FROM CANNED, NS FAT ADDED	75202003
ASPARAGUS, COOKED, FROM CANNED, FAT NOT ADDED	75202013
ASPARAGUS, COOKED, FROM CANNED, FAT ADDED	75202023
BEANS, STRING, CKD, FROM CAN, NS COLOR, FAT ADDED	75204983
BEANS, STRING, CKD, FROM CAN, NS COLOR, NO FAT ADDED	75204993
BEANS, STRING, CKD, FROM CAN, NS COLOR, NS FAT ADDED	75205003
BEANS, STRING, GREEN, COOKED, FROM CANNED, NS FAT ADDED	75205013
BEANS, STRING, GREEN, COOKED, FROM CANNED, FAT NOT ADDED	75205023
BEANS, STRING, GREEN, COOKED, FROM CANNED, FAT ADDED	75205033
BEANS, GREEN, CANNED, LO NA, NS AS TO ADDED FAT	75205110
BEANS, GREEN, CANNED, LO NA, FAT NOT ADDED	75205120
BEANS, GREEN, CANNED, LO NA, FAT ADDED	75205130
BEANS, STRING, YELLOW, COOKED, FROM CANNED, NS ADDED FAT	75206003
BEANS, STRING, YELLOW, COOKED, FROM CANNED, NO FAT ADDED	75206013
BEANS, STRING, YELLOW, COOKED, FROM CAN, FAT ADDED	75206023
BEAN SPROUTS, COOKED, FROM CANNED, NS FAT ADDED	75207003
BEAN SPROUTS, COOKED, FROM CANNED, FAT NOT ADDED	75207013
BEAN SPROUTS, COOKED, FROM CANNED, FAT ADDED	75207023
BEETS, COOKED, FROM CANNED, NS AS TO FAT ADDED	75208003
BEETS, COOKED, FROM CANNED, FAT NOT ADDED	75208013
BEETS, COOKED, FROM CANNED, FAT ADDED	75208023

BEETS, CANNED, LOW SODIUM, NS AS TO ADDED FAT	75208100
BEETS, CANNED, LOW SODIUM, FAT NOT ADDED	75208110
BEETS, CANNED, LOW SODIUM, FAT ADDED	75208120
CAULIFLOWER, COOKED, FROM CANNED, NS FAT ADDED	75214003
CAULIFLOWER, COOKED, FROM CANNED, FAT NOT ADDED	75214013
CAULIFLOWER, COOKED, FROM CANNED, FAT ADDED	75214023
CORN, COOKED, FROM CANNED, NS COLOR, NS FAT ADDED	75216003
CORN, COOKED, FROM CANNED, NS COLOR, FAT NOT ADDED	75216013
CORN, COOKED, FROM CANNED, NS COLOR, FAT ADDED	75216023
CORN, FROM CANNED, NS AS TO COLOR, CREAM STYLE	75216053
CORN, YELLOW, COOKED, FROM CANNED, NS FAT ADDED	75216103
CORN, YELLOW, COOKED, FROM CANNED, FAT NOT ADDED	75216113
CORN, YELLOW, COOKED, FROM CANNED, FAT ADDED	75216123
CORN, YELLOW, FROM CANNED, CREAM STYLE	75216153
CORN, YELLOW & WHITE, COOKED, FROM CAN, NS FAT ADDED	75216163
CORN, YELLOW & WHITE, COOKED, FROM CAN, NO FAT ADDED	75216173
CORN, YELLOW & WHITE, COOKED, FROM CAN, FAT ADDED	75216183
CORN, YELLOW, FROM CANNED, CREAM STYLE, FAT ADDED	75216193
CORN, WHITE, COOKED, FROM CANNED, NS FAT ADDED	75216203
CORN, WHITE, COOKED, FROM CANNED, FAT NOT ADDED	75216213
CORN, WHITE, COOKED, FROM CANNED, FAT ADDED	75216223
CORN, WHITE, FROM CANNED, CREAM STYLE	75216253
CORN, YELLOW, CANNED, LO NA, NS AS TO ADDED FAT	75216300
CORN, YELLOW, CANNED, LOW SODIUM, FAT NOT ADDED	75216310
CORN, YELLOW, CANNED, LOW SODIUM, FAT ADDED	75216320
MUSHROOMS, COOKED, FROM CANNED, NS FAT ADDED	75219003
MUSHROOMS, COOKED, FROM CANNED, FAT NOT ADDED	75219013
MUSHROOMS, COOKED, FROM CANNED, FAT ADDED	75219023
OKRA, COOKED, FROM CANNED, NS FAT ADDED	75220003
OKRA, COOKED, FROM CANNED, FAT NOT ADDED	75220013
OKRA, COOKED, FROM CANNED, FAT ADDED	75220023
ONIONS, PEARL, COOKED, FROM CAN (INCL PICKLED/COCKTAIL)	75221033
PEAS, GREEN, COOKED, FROM CANNED, NS FAT ADDED	75224013

PEAS, GREEN, COOKED, FROM CANNED, FAT NOT ADDED	75224023
PEAS, GREEN, COOKED, FROM CANNED, FAT ADDED	75224033
PEAS, GREEN, CANNED, LOW SODIUM, NS AS TO ADDED FAT	75224110
PEAS, GREEN, CANNED, LOW SODIUM, FAT NOT ADDED	75224120
PEAS, GREEN, CANNED, LOW SODIUM, FAT ADDED	75224130
PEPPERS, HOT, COOKED, FROM CANNED, NS FAT ADDED	75226093
PEPPERS, HOT, COOKED, FROM CANNED, NO FAT ADDED	75226103
PEPPERS, HOT, COOKED, FROM CANNED, FAT ADDED	75226113
SQUASH, SUMMER, COOKED, FROM CANNED, NS FAT ADDED	75233003
SQUASH, SUMMER, COOKED, FROM CANNED, FAT NOT ADDED	75233013
SQUASH, SUMMER, COOKED, FROM CANNED, FAT ADDED	75233023
TURNIP, COOKED, FROM CAN, NS AS TO ADDED FAT	75234003
TURNIP, COOKED, FROM CANNED, FAT NOT ADDED	75234013
TURNIP, COOKED, FROM CAN, FAT ADDED	75234023
MIXED VEGETABLES (CORN,LIMA,PEAS,GRBNS,CAR), CANNED, NS FAT	75311003
MIXED VEGETABLES (CORN,LIMA,PEAS,GRBNS,CAR), CANNED, NO FAT	75311013
MIXED VEGETABLES (CORN,LIMA,PEAS,GRBNS,CAR), CANNED, W/ FAT	75311023
MIXED VEGETABLES, CANNED, LOW SODIUM, NS ADDED FAT	75311100
MIXED VEGETABLES, CANNED, LOW SODIUM, NO FAT ADDED	75311110
MIXED VEGETABLES, CANNED, LOW SODIUM, FAT ADDED	75311120
ASPARAGUS, FROM CANNED, CREAMED OR W/ CHEESE SAUCE	75401013
BEANS, STRING, GREEN, FROM CANNED, CREAMED/CHEESE SCE	75403013
BEANS, STRING, GREEN, CKD, FROM CAN, W/ MUSHROOM SCE	75403023
BEANS, STRING, YELLOW, FROM CANNED, CREAMED/CHEESE SCE	75404013
CAULIFLOWER, FROM CANNED, CREAMED(INCL W/ CHEESE SAUCE)	75409013
CORN, COOKED, FROM CAN, W/ CREAM SAUCE, MADE W/ MILK	75411033
MUSHROOMS, FROM CANNED, CREAMED	75414013
PEAS, FROM CANNED, CREAMED	75417013
PEAS, COOKED, FROM CANNED, W/ MUSHROOM SAUCE	75417023
PEAS, COOKED, FROM CANNED, W/ TOMATO SAUCE	75417033
SQUASH, SUMMER, FROM CANNED, CREAMED	75418053

	TURNIPS, FROM CANNED, CREAMED	75418103
BEANS	BEANS, LIMA, IMMATURE, COOKED, FROM CANNED, NS FAT ADDED	75204003
	BEANS, LIMA, IMMATURE, COOKED, FROM CAN, NO FAT ADDED	75204013
	BEANS, LIMA, IMMATURE, COOKED, FROM CAN, FAT ADDED	75204023
	BEANS, LIMA, IMMATURE, CANNED, LOW SODIUM, NS AS TO FAT	75204100
	BEANS, LIMA, IMMATURE, CANNED, LOW SODIUM, NO FAT ADDED	75204110
	BEANS, LIMA, IMMATURE, CANNED, LOW SODIUM, FAT ADDED	75204120
	PEAS, COW/FIELD/BLACK EYE, NOT DRY, CKD, FROM CAN, NS FAT	75223003
	PEAS, COW/FIELD/BLACK EYE, NOT DRY, CKD, FROM CAN, NO FAT	75223013
	PEAS, COW/FIELD/BLACK EYE, NOT DRY, CKD, FROM CAN, W/ FAT	75223023
	PIGEON PEAS, COOKED, FROM CANNED, FAT NOT ADDED	75225013
	BEANS, LIMA, IMMATURE, FROM CANNED, CREAMED/CHEESE SCE	75402013
	BEANS, LIMA, IMMATURE, CKD, FROM CAN, W/ MUSHROOM SCE	75402023
SOUP	CHEDDAR CHEESE SOUP, CANNED, UNDILUTED	14710110
	BEEF & MUSHROOM SOUP, CANNED, LOW SODIUM (INCL BEEF	28316020
	CHICKEN SOUP, CANNED, UNDILUTED	28340520
	CHICKEN/TURKEY SOUP, CM OF, CAN, RED SOD, NS W/ MILK/WATER	28345010
	CHICKEN/TURKEY SOUP, CM OF, CAN, RED SOD, W/ MILK	28345020
	CHICKEN/TURKEY SOUP, CM OF, CAN, RED SOD, W/ WATER	28345030
	CHICKEN/TURKEY SOUP, CM OF, CAN, RED SOD, UNDILUTED	28345040
	CHICKEN SOUP, CREAM OF, CANNED, UNDILUTED	28345140
	CLAM CHOWDER, CANNED, NEW ENGLAND, RED SODIUM, RTS	28355140
	BEAN & HAM SOUP, CAN, REDUCED SODIUM, W/ WATER/RTS	41601160
	SPLIT PEA SOUP, CAN, REDUCED SODIUM, W/ WATER/RTS	41602070
	SPLIT PEA & HAM SOUP, CAN, REDUCED SODIUM, W/ WATER/RTS	41602090
	BEEF NOODLE SOUP, CANNED, UNDILUTED	58402000
	CHICKEN NOODLE SOUP, CANNED, UNDILUTED	58403020
	CHICKEN NOODLE SOUP, CANNED, LOW SODIUM	58403030
	CHICKEN NOODLE SOUP, CAN, RED SODIUM, READY-TO-SERVE	58403060
	CHICKEN & RICE SOUP, CANNED, UNDILUTED	58404020

	CHICKEN RICE SOUP, CAN, RED SODIUM, PREP W/ WATER/RTS	58404040
	CHICKEN RICE SOUP, CAN, REDUCED SODIUM, W/ MILK	58404050
	TOMATO RICE SOUP, CANNED, UNDILUTED	74605000
	CELERY SOUP, CREAM OF, CANNED, UNDILUTED	75603030
	MUSHROOM SOUP, CANNED, UNDILUTED (INCL CREAM OF)	75607030
	MUSHROOM SOUP, CREAM OF, CAN, RED. SOD., NS W/ MILK/WATER	75607090
	MUSHROOM SOUP, CREAM OF, CAN, RED. SODIUM, PREP W/ MILK	75607100
	MUSHROOM SOUP, CM OF, CAN, RED SOD, PREP W/ WATER	75607140
	MUSHROOM SOUP, CM OF, CAN, RED SOD, UNDILUTED	75607150
	ONION SOUP, CREAM OF, CANNED, UNDILUTED	75608030
	PEA SOUP, CAN, LOW SOD, PREP W/ WATER	75609050
	VEGETABLE SOUP, CANNED, UNDILUTED	75649020
	VEGETABLE SOUP, CANNED, LOW SODIUM	75649030
	MINESTRONE SOUP, CANNED, REDUCED SODIUM, RTS	75650990
	VEGETABLE CHCKEN OR TURKEY SOUP, CANNED, UNDILUTED	75651060
	VEGETABLE CHICKEN SOUP, CAN, LOW SOD, PREP W/ WATER	75651090
	VEGETABLE NOODLE SOUP, CAN, RED SODIUM, PREP W/ WATER/RTS	75651150
	VEGETABLE BEEF SOUP, CANNED, UNDILUTED	75652020
PASTA	LASAGNA W/ MEAT, CANNED	58130013
	RAVIOLI, MEAT-FILLED, W/ TOMATO OR MEAT SAUCE, CANNED	58131323
	RAVIOLI, CHEESE-FILLED, W/ TOMATO SAUCE, CANNED	58131523
	PASTA, W/ TOMATO SAUCE & CHEESE, CANNED	58132113
	PASTA W/ TOMATO SAUCE & MEAT/MEATBALLS, CANNED	58132313
	PASTA W/ TOMATO SAUCE & FRANKFURTERS/HOT DOGS, CANNED	58132713
	TORTELLINI, MEAT-FILLED, W/ TOMATO SAUCE, CANNED	58134613
	TORTELLINI,CHEESE-FILLED,MEATLESS,W/TOMATO SAUCE,CANNED	58134623
	MACARONI OR NOODLES W/ CHEESE, CANNED	58145113
	PASTA, MEAT-FILLED, W/ GRAVY, CANNED	58146200
UNCATEGORIZED	QUAIL EGG, CANNED	31203000
	COCONUT CREAM, CANNED, SWEETENED (INCL COCO LOPEZ)	42402010
	SAUERKRAUT, CANNED, LO NA	75230100

CHAPTER FOUR

Manuscript 2

Formative Research to Inform Bisphenol-A (BPA) Exposure Models of School Meals

Abstract

A growing body of research is demonstrating the potential adverse health effects of chemical contaminants unintentionally introduced into food from its packaging. The trend to package food into smaller, individual, ready-to-eat packages, especially in food marketed to children, puts our younger population at risk of higher exposure to packaging contaminants than adults. The goal of this formative research effort is to gather information about school meal policies, patterns, and packaging details to inform a model of potential bisphenol-A exposure dose of a typical school meal reimbursable by the National School Lunch Program (NSLP) and School Breakfast Program (SBP). A mixed-methods approach was utilized to form a baseline of information about school meals. The methods included semi-structured interviews with stakeholders in food service, ongoing communication with key school food partners, a food service director survey, school kitchen and cafeteria visits, and a literature review for BPA food concentration values.

The qualitative research, including interviews and school site visits, revealed the complexity of the NSLP and SBP administration, the prevalence of pre-packaged foods in school nutrition services, and the expansion of food service programs in school. The quantitative research efforts of the food service director survey discovered that 21% of the meal ingredients are sourced from canned food and the majority of food is served on and with materials with BPA exposure potential. The most popular school meals served are cereal for breakfast and pepperoni pizza for lunch. The literature review showed a lack of BPA concentration research for institution foods.

Background

In the past few years, great attention has been focused on improving school food, re-working meal patterns and updating nutrition standards to ensure that children are receiving essential nutrients and calories and will be better positioned to avoid obesity, heart disease, diabetes, and other chronic diseases later in life (Gordon et al 2007; IOM 2007; IOM 2010). The passage of the Child Nutrition Reauthorization Healthy, Hunger-Free Kids Act of 2010 required the USDA to update their regulations regarding school meals to now include more fruits, vegetables, whole grains, and fat-free and low-fat milk. The new regulations also target reducing sodium, saturated fat, and trans fat levels in school meals (Healthy Hunger-Free Kids Act 2010).

A growing body of research reveals that nutrient analysis is not the only factor in determining the health of food. One focus area is the examination of chemical contaminants unintentionally introduced into food from its packaging. The trend to package food into smaller, individual, ready-to-eat packages, especially in food marketed to children, puts our younger population at risk of higher exposure to packaging contaminants than adults since a larger surface area of the food is in contact with the packaging. Children are also more susceptible to food packaging contaminants as research has shown that children eat ten-times more food per their body weight than adults (Muncke 2011).

There are many compounds known to migrate into food, and the FDA sets a migration limit for these packaging components (Duffy et al. 2006). Of particular interest to school-aged children are endocrine disrupting chemicals (EDC) because their developing bodies are especially vulnerable to hormone disruption. Sometimes only

small changes in hormone activity during development can cause permanent effects (Welshons et al. 2003). Besides affecting reproductive organ development, environmental endocrine disruptors have been shown to influence adipogenesis and obesity (Grun and Blumberg 2009; Janesick and Blumberg 2011; Rubin et al. 2001; vom Saal et al. 2012). There are over 50 EDC's that have been approved for use in food packaging in the United States and the European Union (Muncke 2009). Amongst the EDC's of concern is bisphenol-A (BPA), a synthetic chemical used as a monomer base in manufacturing polycarbonate plastic and as a polymer link in epoxy resins. Residual BPA remains after polymerization, allowing this monomer to migrate into foods it contacts (Goodson et al. 2004; McNeal et al. 2000; Munguia-Lopez and Soto-Valdez 2001; Munguia-Lopez et al. 2005). Higher urinary concentrations of bisphenol-A in children 6-19 years old has been associated with a greater prevalence of obesity (Trasande et al. 2012). In the Center for the Evaluation of Risks to Human Reproduction of the National Toxicology Program's expert panel report, they express "some concern that exposure to Bisphenol A potentially causes neural and behavioral effects." There is also "minimal concern that exposure to Bisphenol A potentially causes accelerations in puberty" (NTP 2008). Lower-income children may be at a greater-risk for BPA exposure. In a recent study, an association was found showing that families with lower income, lower food security, and accessing emergency food assistance had higher urinary concentrations of BPA (Nelson et al. 2012).

Bisphenol-A can enter the food system through migration from polycarbonate plastic bottles, dishes, utensils, and storage containers, the epoxy lining of canned foods and beverages, (Biles et al. 1997b; Brede et al. 2003; Brotons et al. 1995; Goodson et al.

2004; Yang et al. 2011) and from BPA found in paperboard used in food containers (Liao and Kannan 2011; Ozaki et al. 2004). Another area of concern is polyvinyl chloride (PVC) plastic film, or stretch cling wrap, used for food storage. Studies have shown BPA leaching from plastic stretch films, into test water, acetic acid, and olive oil (Lopez-Cervantes and Paseiro-Losada 2003). BPA is an additive in food packaging PVC films and in PVC products to eliminate excess hydrochloric acid occurring during manufacturing (Cao et al. 2010). In addition to food, BPA exposure can occur from multiple other pathways. BPA can be measured in household dust, indoor and outdoor air (Wilson et al. 2003; Wilson et al. 2007), water (Lee et al. 2004; Sajiki and Yonekubo 2002), thermal receipts (Geens et al. 2012; Liao and Kannan 2011), recycled paper (Ozaki et al. 2004), from dental sealants (Joskow et al. 2006; Olea et al. 1996) and some medical devices (Calafat et al. 2009). The main BPA exposure pathway is from dietary ingestion, accounting for 99% of total exposure in preschoolers (Wilson et al. 2007) and 74 – 88% for children 6-12 year olds (von Goetz et al. 2010).

One area of food contamination from packaging that has not been well researched in the United States is school meals. Some research has been conducted in school meals in Japan, confirming the existence of BPA leaching into the food from food packaging and tableware (Miyamoto and Kotake 2006; Yamano et al. 2008). This is a worthwhile area of research since, in the U.S., nearly 34 million children eat lunches from the National School Lunch Program every school day. Over 22 million of those children, due to their family's income level, receive their lunch for free or at a reduced price (Food Research and Action Center 2010). School children also receive snacks in after-school and enrichment programs through the National School Lunch Program (USDA 2010).

More than 12 million children ate breakfast through the School Breakfast Program every day in Fiscal Year 2011. Of these children, over 10.1 million of them received their meals free or at a reduced-price (USDA 2012). Research shows reason for concern about children's exposure to BPA from school meals. In a study of the National Health and Nutrition Examination Survey (NHANES) 2005-2006 Food Frequency Questionnaire data, higher urinary BPA concentrations were found to be associated with reported consumption of school lunches (Lakind and Naiman 2011).

Research Questions

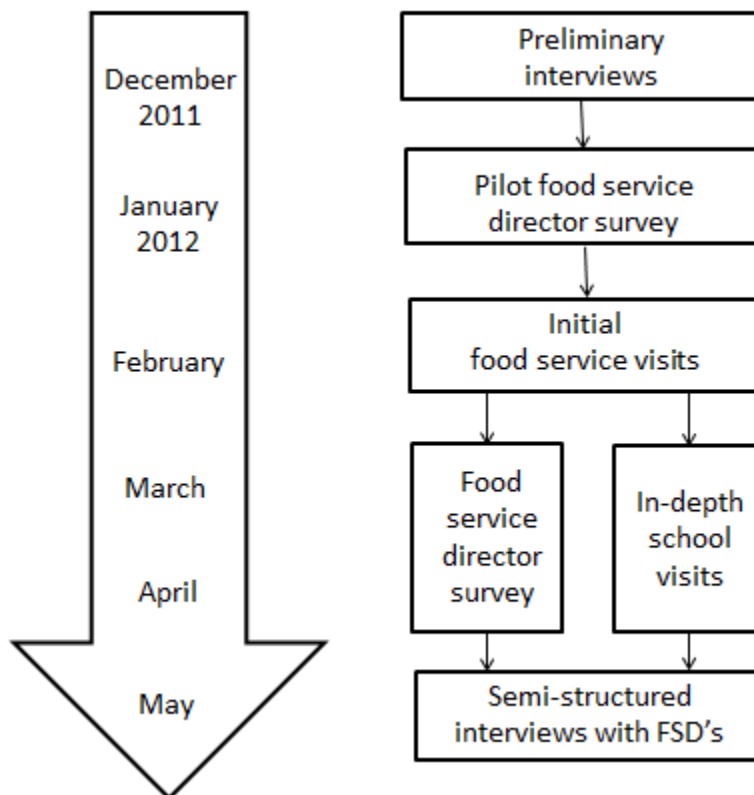
The goal of this formative research effort is to gather information about school meal policies, patterns, and packaging details to inform models of potential bisphenol-A exposure doses of school meals from a school that participates in the National School Lunch Program (NSLP) and School Breakfast Program (SBP). A mixed-methods approach will be utilized to form a baseline of information about school meals. This research focused on answering the following questions:

1. What is the packaging of school meal ingredients?
2. How are school meals prepared?
3. What types of materials are school meals served on/eaten with?
4. What is the most typical school breakfast and lunch served?
5. What are the barriers to removing packaging from school meals?

Methods

The formative research used a mixed-methods approach including semi-structured interviews with stakeholders in school food service, ongoing communication with key school food partners, a food service director survey, school kitchen and cafeteria visits, and literature review for BPA food concentration values. **Figure 4.1** illustrates the mixed-methods utilized in this research.

Figure 4.1 Mixed-Methods and Timeline for Formative Research for BPA School Meal Exposure Models



The informants were drawn from a variety of important stakeholders in school nutrition. The semi-structured interviews were performed with CEO's, food service directors, chefs, dieticians, and lunch room personnel. The following entities were involved in these interviews:

- Baltimore City Public Schools, Baltimore, Maryland
- Chartwells, New York, New York
- Revolution Foods, Oakland, California
- Santa Catalina School, Monterey, California
- Mountain View Whisman School District, Mountain View, California
- Redwood City School District, Redwood City, California

One time semi-structured phone interviews were performed with the dietician from the Baltimore City Public Schools and Chartwells. An in-person semi-structured interview and facility tour was conducted with Revolution Foods. In-person semi-structured interviews followed by school food preparation and service observation were completed at the Santa Catalina School, Landels Elementary, John Gill Elementary, Crittenden Middle School, and Garfield Academy. A semi-structured interview and ongoing e-mail communication was achieved with the food service directors of the Mountain View-Whisman School District and the Redwood City School District.

Stakeholder interviews provided the basis of the food service director survey. The survey was structured to collect information from school nutrition personnel about food preparation practices including questions regarding canned versus fresh foods, food heating practices, food serving containers, and the most common meals served. Before the survey was delivered to a wider audience, a pilot survey was administered to five people in school food service. The goal of the pilot survey was to confirm survey length, the scope and accuracy of questions, and use of appropriate industry language. Their

feedback was applied and was valuable in tailoring the survey to its intended population. A copy of the Pilot Food Service Director Survey can be found in **Appendix A**.

The target population of food service directors (FSDs) was contacted to answer the survey by two different methods. The first method generated a stratified random sample of food service directors from around the country for direct contact by the research staff. The first step was to assemble a list of all school districts in the United States. Next, this list was stratified by state, and then each state district list was randomized. The top ten districts per state were selected and then the contact information for the food service directors was researched from the internet. These food service directors were contacted by phone when possible and then e-mailed the survey link. Voicemails were left when no direct contact was made. If no phone number was available, the food service director was sent an e-mail with a survey link without any pre-notification. An e-mail with a survey link was successfully sent to 232 FSD's from 24 states and the District of Columbia. A follow-up e-mail was administered one week after the initial contact to encourage completion of the survey.

The second method of contacting the survey audience was to advertise the online survey through the USDA listserv, Mealtalk. Mealtalk is a listserv that functions as a national forum for child nutrition professionals to exchange ideas and share ideas about day-to-day operations. Its membership is limited to persons who actively work in school nutrition services (USDA 2013). A short letter requesting people to take the survey was posted on the listserv one time. There was no follow-up communication posted on the listserv.

The survey was developed and administered through an online survey tool (SurveyMonkey, Palo Alto, CA). An incentive was advertised in the survey letter for a \$50 Amazon gift certificate to be awarded to one survey participant through a raffle managed by a third party to SurveyMonkey. All surveys were completed anonymously. Answers to the questions about the most popular school lunch, most popular school breakfast, and food contact materials were used to inform the exposure dose models. To view the Final Food Service Director Survey, see **Appendix B**.

Further data for the exposure model was gathered from school food service site visits. This field work served to inform the model about the meal patterns, types of foods eaten, and meal serving methods. **Table 4.1** describes the school meal service sites that were observed. The types of sites that were visited included a central school meal manufacturing facility for a private company, the full-service kitchen of a private boarding and day school, a central kitchen for a small public elementary and middle school district, and the kitchens and cafeterias of individual public elementary and K-8 schools.

Table 4.1: School Meal Service Site Visits

Name	Institution Type	Grade Level	Kitchen Type	Ingredient Type	Audience
Revolution Foods	Private Company	Serving all grade Levels	Commissary	From Scratch	80% free/reduced lunch
Santa Catalina School	Private School	K-12	On-site facilities	From Scratch	self-paying
Landels Elementary	Public School	K-5	Heating, refrigeration only	Pre-cooked proteins, pre-packaged foods, scratch	43 % free-reduced
Crittenden Middle	Public School	6-8	Warming kitchen; serving all district elementary schools and middle school	Pre-cooked proteins, pre-packaged foods, scratch	56% free-reduced
John Gill Elementary	Public School	K-5	Warming kitchen, for on-site service	Pre-cooked proteins, pre-packaged foods, scratch	68% free-reduced
Garfield Academy	Public School	K-8	Warming kitchen, for on-site service	Pre-cooked proteins, pre-packaged foods, scratch	Free (91% qualified for free/reduced)

Qualitative Research Findings

This research's field work in public school nutrition services revealed the complexity of school meals and their need to balance bureaucratic requirements with the challenges of daily operations. In order to meet the budget needs as well as provide adequate food for students that meet federal reimbursement requirements, schools have largely moved to a system that outsources meal preparation, utilizes federal commodities, and heavily relies on individually packaged foods. This often results in bare-bones kitchen staff, unsavory meals, and kitchens full of pre-prepared foods packaged in plastic. In some schools the only food that could be found that was free of plastic packaging was milk and fresh fruit. The research's original primary aim was to determine what percent of school meals were coming from a can. As research commenced, the focus needed to be expanded to an examination of all types of school food packaging, including the pervasive use of plastics.

An ongoing trend in the U.S. is the expansion of the School Breakfast Program. In the schools observed in this research, the increased serving of breakfast in schools could intensify food packaging exposure. The number of students eating breakfast is more variable than lunch, leading to food service personnel utilizing many breakfast foods in individual packages. For instance, pre-packaged food allows staff to accommodate quickly a sudden influx of students, such as occurs for second breakfast served during recess on rainy days. The individual packages also allow the foods to be restocked if students do not show up for breakfast due to a late bus, in-class snack, or a sunny day. Examples of popular foods served at breakfast that are wrapped in individual, ready-to-eat packages are cold cereals, muffins, breakfast cookies, and sweet potato

cinnamon rolls. The muffins and cinnamon rolls are individually wrapped and heated up in their plastic wrapping. Other common breakfast foods like French toast sticks, pancakes, and waffles, arrive pre-made to the schools in bulk plastic bags. There is concern about plastic food packaging because studies have shown BPA migration from PVC plastic stretch wrap (Lopez-Cervantes and Paseiro-Losada 2003), and estrogenic activity from cheese wrapped in plastic (McNeal et al. 2000). One study found estrogenic activity in all of the plastic food containers they studied (Yang et al. 2011). Further research needs to be conducted regarding the plastics used to package institutional foods. Concern may be premature as a study of household size frozen vegetables showed no detectable levels of BPA (Noonan et al. 2011).

During the field research at schools, an inventory of all of the school food and food packaging was catalogued. In one school, of the 55 types of food that were inventoried from the pantry, refrigerator, and freezer, only 7 of those items were not packaged in plastic or in a can. These items were milk and orange juice in cardboard containers, fresh, whole bananas, apples, and oranges, raisins packaged in a cardboard box, and tuna packaged in vacuum-sealed foil pouches.

A welcomed surprise was that all of the schools observed offered a salad bar. The irony in the school salad bar is that its contents are mostly from cans or plastic bags. At one K-8 school that was visited, the school salad bar contained eight different items: corn, black beans, jalapeño peppers, carrot sticks, jicama sticks, cucumber slices, salad mix, and canned peaches. Of those eight items, only one, the cucumber slices, was fresh prepared on-site. The corn, beans, and jalapeños were from a can. The carrot sticks, jicama sticks, and salad mix come to the school in a plastic bag, pre-washed, and cut in

ready to eat pieces. The cucumbers are delivered to the school whole in a plastic bag and the kitchen staff needs to slice them. The kitchen personnel reported that the reason that the cucumbers are not delivered pre-cut is because the slices are easily damaged during transport. For service, salad bar ingredients are placed in plastic containers that are then placed into the plastic salad bar.

One issue limiting the preparation of more fresh, unprocessed food is that many schools only have a warming kitchen. This means there is limited capacity in cooking foods from scratch and also rules governing what types of food preparation are allowed to take place. Pre-cooked proteins are necessary if the kitchen is only a warming kitchen. An additional reason for using pre-cooked proteins, as evidenced by the results of this research's survey, is that foodborne illness is the main concern for most school nutrition operations. The fear of accidentally sickening the children from microbiological contamination such as *E. coli*, has led food to be increasingly pre-cooked and individually packaged. This has resulted in the pervasive use of pre-cooked proteins. Furthermore, pre-cooked proteins are convenient, requiring little preparation time. This added expediency is necessary for school kitchens that have limited kitchen staff.

Another benefit of pre-cooked proteins is this food type allows schools to take advantage of commodity foods. School districts are allotted a certain amount of commodity food dollars depending on how many students are qualified for free or reduced meals. Commodities are foods that are surplus in the U.S. food supply. There is a constant stream of commodities that come available for purchase through the federal system. The challenge in using commodities is that it is unpredictable what foods may become available and also when the food will be delivered to the school after ordering.

An economical choice is to apply these funds to purchase commodity proteins. Meats are readily available through the commodity system. Use of pre-cooked, frozen proteins also allows the kitchen to be able to freeze the commodities for later use, lessening the issue of predictability of delivery of the goods. A possible issue with the use of pre-cooked proteins and food contact contamination is that all of these proteins come in bulk, plastic packaging. There is also no control over how many other food contact contaminants have been introduced during the food processing.

A further aspect that adds complexity to school food service is the need to be flexible in the numbers of students who will need to be served at any given meal. In a site visit to a K-8 school where the whole student population is eligible to eat school meals for free, the staff expressed the difficulty in feeding such a variable number of students. In these situations, the staff needs to be able to have food that is pre-packaged and or cold so that it can be served quickly to feed a sudden influx of students. On the day I observed the school kitchen, it was a rainy day. At the first recess, the “second breakfast” is served. This breakfast service is in addition to the breakfast served before school. Any child who did not make it to the before school breakfast is welcome to receive breakfast during recess. As predicted by the staff, there was an influx of students who came to get breakfast because it started to rain at recess and the kids were not allowed to play outside in the yard. This rain caused the breakfast service needs to significantly increase. The final tally for breakfast was 550 meals, when the usual is 420. On days like this, flexibility in food service is essential. The breakfast foods need to be able to be quickly placed out in the service line during meal time. If not eaten, the foods then need to be

able to be returned to the shelves to be eaten at a later time. This can be accomplished if the foods are packaged and shelf-stable.

Quantitative Research Findings

The response rate for the food service director survey far exceeded expectations for an online survey to unknown entities. The research team anticipated a response rate of less than 20%. The overall response rate was 49% (113/232). For persons who were contacted by phone before the e-mail link was sent to them, the response rate was 62.5% (80/128). This number includes people that spoke to the research staff directly, received a voicemail, or were left a message from their administrative assistant or co-worker. For e-mail contact only, the response rate was 32% (33/104). 59 additional surveys were completed from the Mealtalk listserv. Response rate cannot be calculated for this population since it is unknown how many people viewed the request to complete the survey.

Analysis was conducted to characterize the survey respondents. Using the zip codes associated with the school districts of the respondents, it was discovered that the survey participants were from a fairly balanced range of population densities. School zip codes of respondents were put into different groups according to census designations. The results of the analysis are: 51 % (35/69) of the zip codes of respondents were from an urban area, designated as an MSA, Metro Division, or Micro division. Forty-one percent (28/69) of respondents were from zip codes in a rural area. The remaining respondents, 9% (6/69), were from school districts whose zip codes are non MSA with an MSA hub. As expected, almost all of the survey respondents were from public schools (99.4% or 170/171). K-12 districts were represented by 78.5% of respondents.

A background survey question determined who made the menu choices in the school district. In the majority of respondents (65.7%), the food service director

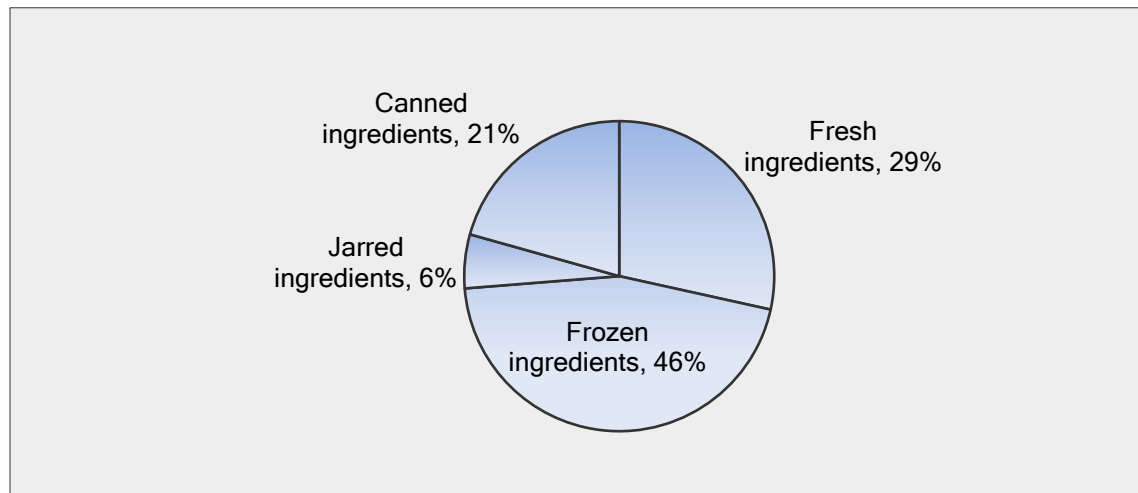
determined the menu choices. Fourteen percent of the districts have their menus determined by a nutritionist, and another 14.5% have menu choices influenced by the food service director, dietitian, and students. Only 4.1% of schools have menus determined by the school kitchen staff. Consultants to the school districts contribute 1.7% of menu choices.

When asked to rank their concerns regarding school meals, food service directors marked foodborne illness as their main concern. Nutrition and taste were the second and third ranked concern. The other worries, in rank from most concerning to least, were: portion size, food contaminants, and packaging waste. The other concerns written into the survey were competing interests, bad press about school meals, and food availability for the school's geographic region.

According to the survey, most school meals are prepared on-site, with 89.6% of responses selecting this option. On-site preparation was described in the survey as including use of individual ingredients such as pre-cooked proteins, pre-cut produce, and canned or frozen foods. A little over 10% of school meals are a combination of on-site preparation and pre-plated meals. None of the respondents serve all pre-plated meals.

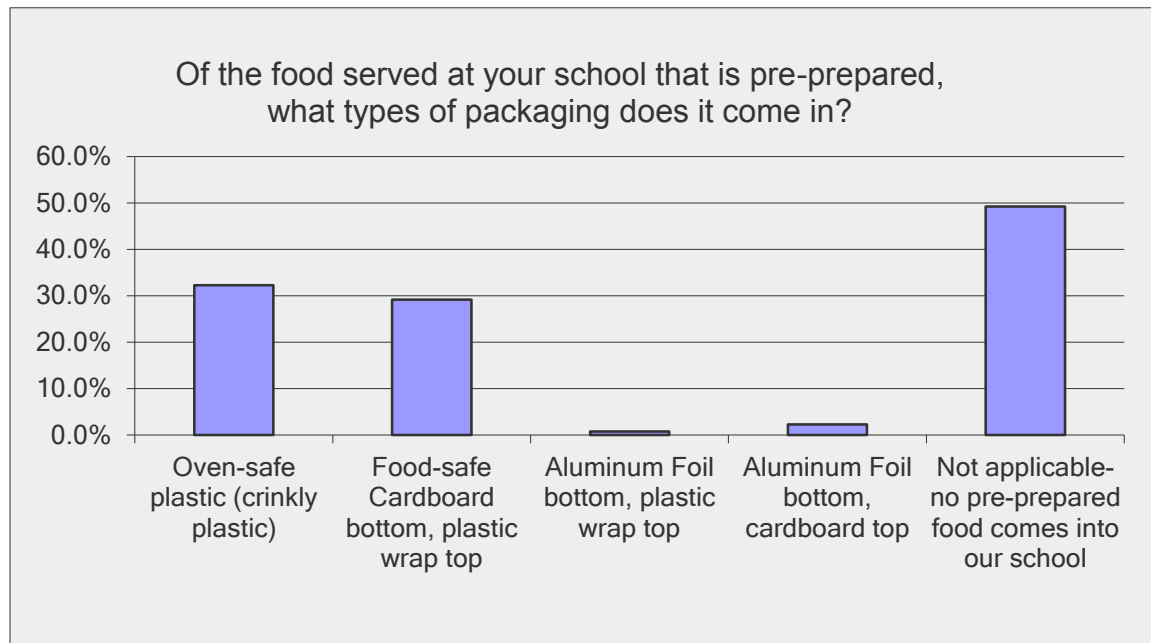
The remaining survey questions were designed to inform the exposure modeling. Food service directors were asked about the types of individual ingredients used in preparing the school meals. As shown in **Figure 4.2**, almost half of ingredients are frozen, 29% are fresh ingredients, 21 % are canned, and 6% are jarred.

Figure 4.2 School Meal Ingredients by Packaging Type



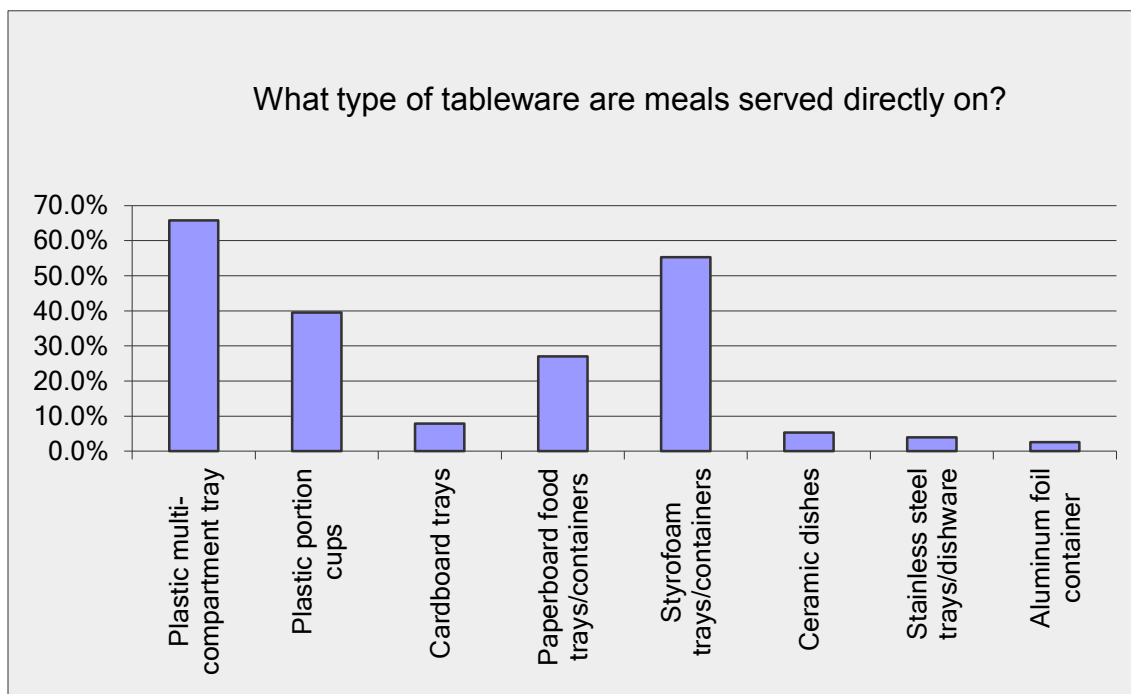
It was also important to assess the types of packaging from which the pre-plated school meals are served. Almost a third of the pre-prepared foods served in the surveyed schools were packaged in oven-safe plastic. Twenty-nine percent of the school meals are served in food-safe cardboard with plastic on top. A small percent of meals are served in aluminum foil containers with either a cardboard covering or a plastic covering. The respondents had an option to write in responses. There was a variety of other packaging reported, including frozen food in plastic bags that are re-heated in steamer pans, frozen bulk items that are removed from plastic bags before re-heating on sheet pans, plastic bags of food in cardboard boxes where plastic is removed before heating, and food that comes to the school from a central kitchen in stainless steel hotel pans. **Figure 4.3** displays the school meal packaging survey results. When food is heated in the school kitchens, an oven is used 83% of the time. A stove is used 16% of the time to heat food. A microwave is only used 1% of the time.

Figure 4.3: Pre-Prepared School Meal Packaging



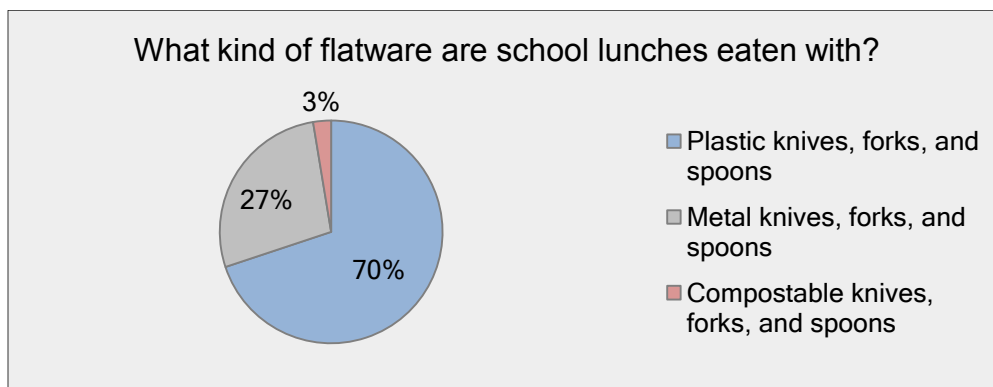
Survey takers were questioned about the material that the school meal came directly in contact with, choosing all types of serving ware utilized at their school. Two-thirds of responses reported using plastic multi-compartment trays to serve their meals. Fifty-five percent use Styrofoam trays and containers to serve their meals. Twenty-seven percent use paperboard food trays to serve their food. **Figure 4.4** displays all of the serving ware options and the percent of responses for each.

Figure 4.4: School Meal Food Contact Material



Since polycarbonate flatware has been documented as another source of BPA, the survey inquired about the types of flatware used in schools. In the majority of the locations, schools are using plastic knives, forks, and spoons. Metal flatware is utilized 27% of the time. Three percent of schools reported using compostable flatware. These results are displayed in **Figure 4.5**.

Figure 4.5: School Meal Flatware



When food service directors were questioned about their top three selling lunch items, the responses were pepperoni pizza, cheese pizza, and chicken tenders. The top three selling breakfast items were cereal, French toast sticks, and pancakes. Breakfast is being served in 95% of the schools surveyed, much higher than expected since 34 million children eat a school lunch and through the NSLP and 12 million eat school breakfast from the SBP every day. Due to the fact that survey respondents are school districts that serve lunch, this number is quite comparable to research that found that 88% of schools serving lunch also serve breakfast (Food Research and Action Center 2010). This shows that even though almost the same numbers of schools participate in the federal school breakfast and school lunch programs, the participation per school is much higher for lunch than breakfast.

Discussion

This article presented the formative research for modeling the potential BPA exposure from school meals. The research successfully integrated mixed-methods approaches to gather data points for the exposure modeling exercise. Through interviews, school site visits, a food service director survey, and literature review, the formative research answered the research questions about school meal packaging, preparation, and service. It also determined the most popular school meals and identified the barriers to removing packaging from school meals. The food service director survey confirmed that the majority of schools that serve lunch also serve breakfast (Food Research and Action Center 2010). The research presented here has been incorporated into BPA exposure dose models for school breakfast and lunches.

Strengths found in the food service director survey were that it gathered responses from across the country, the school district survey takers were from an even mix of urban and rural locations, and the responders were the decision makers for the districts' school meals. The schools visited represented a variety of income backgrounds for public schools receiving support from the National School Lunch Program. The ongoing relationships built with the food service directors enriched the researcher's understanding of complexity of school lunch service and federal reimbursement guidelines.

This research to explore the sources of BPA exposures in school meals is the first known of its kind in the United States. Other known research efforts are two studies of school food and BPA exposure from Japan. The school nutrition services of Japan, including the foods, dishes, and eating utensils, differ greatly from the United States. Due to this, direct comparison was not feasible. These studies remained useful to give

direction to this research, guiding investigation of exposure sources in United States equivalents (Miyamoto and Kotake 2006; Yamano et al. 2008).

A limitation of this research is that the school observations were all conducted in California schools. Although funding for the National School Lunch Program and the School Breakfast Program are from the federal level, programs are administered at the state level leading to possible differences. Generalizability to the rest of the country because all states must follow the same federal guidance for a reimbursable meal, and all states, except Alaska and Hawaii, receive the same amount of money for each reimbursable meal served. The federal commodities selection available is the same for all states. The remaining non-commodities food purchased could lead to potential regional difference in foods procured.

Another limitation of the study is that the public school site visits were all conducted at locations with meal programs supported by the National School Lunch Program and the School Breakfast Program. Sometimes small districts and ones that only have a few percent of their students qualifying for free or reduced price lunches decide to not have a their meal service run by the NSLP because it is not cost effective. The meal services in these types of schools were not investigated. A private school where all students were self-paying for school meals was included as part of the investigation for comparative purposes.

Conclusions

This study provides valuable insight into school meal structure, service, and packaging that can be used for the basis of exposure assessment work. The food service director survey and school site observations showed that school meal components largely come to schools in plastic bags, are served onto plastic trays, and eaten with plastic utensils. To better estimate BPA exposures in school meals and other institutional settings, future formative research should work to document the sources of food contact experienced in school cafeterias. Further research could analyze the frequency of potential BPA contamination of food from contact with paperboard serving trays and from use of paper napkins. Another aspect of school meal BPA exposures that have not been addressed are the unique foods served in schools. Institutional food preparation is distinct because it utilizes larger sized canned goods, uses bulk pre-cooked proteins, bulk pre-prepared meals, and also employs many individually packaged foods. Analysis of this pattern of food service is a valuable endeavor.

From this research's observations and analysis, schools are on the right track in some areas for reducing packaging and BPA exposure. There should be continued support of efforts designed to increase fresh foods in schools such as the National Farm to School program, and the Let's Move Salad Bar to School, a public-private partnership program (Harris et al. 2012; USDA 2013). In schools that already have a salad bar, besides the substitution of canned foods with fresh, additional ways for potential sources of EDCs to be removed from this service area would be to substitute the plastic serving dishes and utensils commonly used. Salad bar ingredients could be placed in stainless

steel metal containers instead of plastic. The serving utensils could also be substituted with metal serving spoons and tongs.

Other feasible fixes to reduce BPA in school meals, ones that do not require significant capital investment or labor costs, could be to focus effort to convert the purchase of canned foods to fresh or frozen fruits and vegetables. A likely challenge to reducing canned foods is perishability. Possible solutions include additional support for local sources of fresh food to reduce travel time and increase shelf life at the school. Increasing frozen foods might meet the challenge of the greater need for freezer space. Due to their need to store commodity goods that come at irregular intervals, most schools are already equipped with large freezers. More frequent deliveries or more reliable delivery of commodity foods might remove the need to purchase additional freezers.

A key to a broader reduction to packaging in schools is through education. As the food service director survey revealed, cost, taste, and nutrition of school meals are much higher priorities than contaminants from food packaging. Education efforts can slowly introduce the food service personnel to the potential hazards of endocrine disrupting chemicals such as BPA. Once school nutrition professionals know more about endocrine disrupting chemicals, BPA, and how these chemicals potentially play a role in increasing health risks to diseases such as childhood obesity, their openness to packaging reduction strategies will increase.

Although focus of this formative research was to learn more about potential sources of BPA exposures in school meals, there needs to be a broader focus on all of the chemicals and indirect additives from packaging, be it from paper or plastic. A growing body of research shows the many sources of endocrine disrupting chemicals migrating

into food (Duffy et al. 2006; Lopez-Cervantes and Paseiro-Losada 2003; Lopez-Espinosa et al. 2007; McNeal et al. 2000; Muncke 2009; Ozaki et al. 2004). Regulatory agencies are examining their current scientific opinion and regulatory frameworks governing endocrine disrupting chemicals. This action confirms the need to magnify research efforts towards this class of chemicals that can disproportionately affect the youngest and most vulnerable in our population.

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APPENDIX A: Pilot Food Service Director Survey

School Lunches

1. Which job description most closely matches yours?

- ☐ Food Service Director of an elementary school
- ☐ Food Service Director of a middle school
- ☐ Food Service Director of an elementary/middle school district
- ☐ Food Service Director of a high school
- ☐ Food Service Director of a high school district
- ☐ Food Service Director of a K-12 school
- ☐ Food Service Director of a K-12 school district
- ☐ Other job description

2. Where are school meals for your school/district prepared?

- ☐ On-site preparation (cooked in kitchen from scratch ingredients)
- ☐ Meals are prepared off-site and served/re-heated at school
- ☐ Meals are a combination of scratch cooking and pre-prepared meals

3. Who determines the school menu items?

- ☐ As food service director, I do.
- ☐ The choices are made by a consultant.
- ☐ The choices are made by a nutritionist.
- ☐ The choices are made by the school kitchen staff.
- ☐ Other person choosing menu items

4. Please enter the percentage of menu items prepared from the following types of foods:

Frozen ingredients	<input type="text"/>
Fresh ingredients	<input type="text"/>
Jarred ingredients	<input type="text"/>
Canned ingredients	<input type="text"/>

5. Of the food served at your school that is pre-prepared, what types of packaging does it come in?

Foil bottom, cardboard top	<input type="text"/>
Foil bottom, plastic wrap top	<input type="text"/>
Cardboard bottom, plastic wrap top	<input type="text"/>
Plastic wrapped (crinkly plastic)	<input type="text"/>

6. Of the food served at your school(s) that is pre-prepared, what percent of the time are each method of heating used?

Microwave	<input type="text"/>
Stove-top	<input type="text"/>

**7. What type of tableware are meals served directly on?
(question about the flatware used is separate)**

- ☐ Plastic multi-compartment tray
- ☐ Stainless steel dishware
- ☐ Styrofoam
- ☐ Cardboard trays
- ☐ Ceramic dishes

8. What kind of flatware are school lunches eaten with?

- ☐ Plastic knives, forks, and spoons
- ☐ Metal knives, forks, and spoons
- ☐ Compostable knives, forks, and spoons


9. What are your top three selling main dishes? (please select three of the following choices)

- ☐ Cheese Pizza
- ☐ Corn Dogs
- ☐ Grilled cheese
- ☐ Hamburgers
- ☐ Bean Burritos
- ☐ Fish sticks
- ☐ Meat Burritos
- ☐ Chicken nuggets
- ☐ Hot Dogs
- ☐ Pepperoni Pizza
- ☐ Veggie burgers
- ☐ Please add description of top selling menu item if not on list provided

10. Please rank what aspects of school lunch you are concerned with:

- ☐ Packaging waste
- ☐ Portion size
- ☐ Cost
- ☐ Taste
- ☐ Nutrition
- ☐ Food Safety: Biological (For example, E.coli or salmonella contamination)
- ☐ Food Safety: Chemical (For example, Bisphenol-A or pesticide residues)
- ☐ Other school lunch concern aspects

APPENDIX B: Final Food Service Director Survey

Exit this survey

School Lunch Survey
Introduction to Survey and Background Questions

17%

Welcome to our School Lunch Survey!

This survey is designed to be taken by Child Nutrition Program Directors, Food Service Directors, and Head Cooks.

Its purpose is to provide our research project with information to model a student's potential exposure to chemical contaminants, such as Bisphenol-A (BPA), from their school meal. Exposure could take place from the contaminated meal ingredients, the packaging, and/or the serving materials.

This survey will take approximately five minutes to complete. All responses are anonymous.

1. Which job description most closely matches yours?

☐ Food Service Director of an elementary school/school district

☐ Food Service Director of a middle school/school district

☐ Food Service Director of a high school/school district

☐ Food Service Director of a K-12 school/school district

☐ Other job description

2. Is the school/school district public or private?

☐ Public (including charter schools)

☐ Private

3. Who determines the school menu items?

☐ The choices are made by a nutritionist.

☐ The choices are made by a consultant.

☐ The choice are made by the food service director.

☐ The choices are made by the school kitchen staff.

☐ Other person choosing menu items

Next

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The following questions are designed to gather details about the school meal preparation, packaging, and serving process.

4. Where are school meals for your school/district prepared?

- ☐ On-site preparation (cooked in kitchen from individual ingredients- this includes pre-cooked proteins, pre-cut produce, canned and frozen products)
- ☐ Meals come to the school pre-plated and served/re-heated at school
- ☐ Meals are a combination of on-site cooking and pre-plated meals

5. Please enter the percentage of menu items prepared from the following types of foods:

Jarred ingredients	<input type="text"/>
Frozen ingredients	<input type="text"/>
Canned ingredients	<input type="text"/>
Fresh ingredients	<input type="text"/>

6. Of the food served at your school that is pre-prepared, what types of packaging does it come in?

- ☐ Aluminum Foil bottom, plastic wrap top
- ☐ Oven-safe plastic (crinkly plastic)
- ☐ Aluminum Foil bottom, cardboard top
- ☐ Food-safe Cardboard bottom, plastic wrap top
- ☐ Not applicable- no pre-prepared food comes into our school

If another type of packaging is used, please describe here.

7. Of the food served at your school(s) that is pre-prepared, what percent of the time are each method of heating used?

Microwave	<input type="text"/>
Stove-top	<input type="text"/>
Oven	<input type="text"/>

8. What type of tableware are meals served directly on?
(food comes in contact with this product)

Note: question about the flatware used is separate

- ☐ Paperboard food trays/containers
- ☐ Cardboard trays
- ☐ Styrofoam trays/containers
- ☐ Plastic portion cups
- ☐ Stainless steel trays/dishware
- ☐ Ceramic dishes
- ☐ Plastic multi-compartment tray
- ☐ Aluminum foil container

9. What kind of flatware are school lunches eaten with?

- ☐ Metal knives, forks, and spoons
- ☐ Plastic knives, forks, and spoons
- ☐ Compostable knives, forks, and spoons

Prev

Next

School Lunch Survey

School Meals

50%

10. What are your top three selling lunch main dishes? (please select three of the following choices)

	1	2	3
Bean Burritos	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Corn Dogs	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Veggie Burgers	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Hamburgers	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Fish Sticks	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Grilled Cheese	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Beef Tacos	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Cheese Pizza	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Chicken Tenders	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Pepperoni Pizza	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Hot Dogs	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Pasta with tomato sauce	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Other	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Please add description for "Other" choice selected above

11. Do you serve breakfast at your school/school district?

- ☐ Yes
☐ No

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School Lunch Survey

School Breakfast

67%

12. What are your top three selling breakfast main dishes? (please choose three)

* If breakfast is not served at your school/school district, please write in "Not Applicable" below.

	1	2	3
Egg Sandwich	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pancakes	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Breakfast Burrito	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Cereal	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Ham and Eggs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Waffles	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
French Toast Sticks	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Please add description for "Other" Breakfast item or "Not Applicable" if no breakfast is served.

Last question!

13. Please rank the following aspects of school meals with your level of concern:
(1 is most concerned, 8 least concerned)

	1	2	3	4	5	6	7	8
Packaging waste	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Foodborne illness: (For example, E.coli or salmonella contamination)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Nutrition	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Portion size	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Food Contaminants: (For example, Bisphenol-A, phthalates, pesticide residues)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Taste/student preference	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Cost	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Other	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>



[Exit this survey](#)

School Lunch Survey

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Thank you for your time in taking this survey!

Your investment in this research project is greatly appreciated.

Sincerely,
Jennifer Hartle
Johns Hopkins University
Bloomberg School of Public Health
Doctoral Candidate

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CHAPTER FIVE

Manuscript 3

Probabilistic and Deterministic Modeling of School Meals for Potential BPA Exposure

Abstract

Objectives: A growing body of research is demonstrating the potential adverse health effects of chemical contaminants unintentionally introduced into food from its packaging. Of particular interest to school-aged children are endocrine disrupting chemicals (EDC) because their developing bodies are especially susceptible to hormone disruption. Amongst the EDC's of concern is bisphenol-A (BPA), a synthetic chemical used in the manufacturing of polycarbonate plastic food containers and epoxy resin linings of canned food and beverages. BPA is one over 50 EDC's that have been approved for use in food packaging in the United States and the European Union (Muncke 2009). Residual, unreacted BPA from the manufacturing process can migrate into the foods it contacts (Goodson et al. 2004; McNeal et al. 2000; Munguia-Lopez and Soto-Valdez 2001; Munguia-Lopez et al. 2005). The goal of this research is to model the potential exposure dose of bisphenol-A migrating from packaging into food served in a typical school meal. The meal is modeled after the food service of school that participates in the National School Lunch Program (NSLP) and School Breakfast Program (SBP).

Methods/Study Design: Deterministic and probabilistic exposure models for school breakfast and school lunch were informed by data collected from key food service personnel interviews, a food service director survey, school site visits, and published BPA food concentration values. Exposure scenarios included meals with low, moderate, and high levels of canned and packaged food exposure. Intake values were based on the NSLP and SBP guidelines and incorporated plate waste potential.

Results: The potential BPA exposure was modeled with a range starting at 7.7×10^{-4} $\mu\text{g}/\text{kg-BW}/\text{day}$ for the minimum low exposure breakfast for a 6th-8th grader with

average plate waste to a high of 0.97 $\mu\text{g}/\text{kg-BW}/\text{day}$, for the maximum high potential exposure meal consumed during lunch for a K-5 student.

Conclusions: The modeled BPA exposure doses from school meals are low in comparison to the RfD of 50 $\mu\text{g}/\text{kg-BW}/\text{day}$ determined by the EPA to be a safe chronic exposure level for BPA. Research performed since the development of the RfD demonstrates that the threshold for animal toxicity is as low as 2 $\mu\text{g}/\text{kg-BW}/\text{day}$. Many of the doses modeled in this research exceed this toxicity threshold, illustrating the potential for school meals to place children at risk for toxic exposures to BPA.

Background

In the past few years, great attention has been focused on improving school food, re-working meal patterns and updating nutrition standards to ensure that children are receiving essential nutrients and calories and will be better positioned to avoid obesity, heart disease, diabetes, and other chronic diseases later in life (Gordon et al 2007; IOM 2007; IOM 2010). The passage of the Child Nutrition Reauthorization Healthy, Hunger-Free Kids Act of 2010 required the USDA to update their regulations regarding school meals to now include more fruits, vegetables, whole grains, and fat-free and low-fat milk. The new regulations also target reducing sodium, saturated fat, and trans fat levels in school meals (Healthy Hunger-Free Kids Act 2010).

A growing body of research reveals that nutrient analysis is not the only factor in determining the health of food. One focus area is the examination of chemical contaminants unintentionally introduced into food from its packaging. The trend to package food into smaller, individual, ready-to-eat packages, especially in food marketed to children, puts our younger population at risk of higher exposure to packaging contaminants than adults since a larger surface area of the food is in contact with the packaging. Children are also more susceptible to food packaging contaminants as research has shown that children eat ten-times more food per their body weight than adults (Muncke 2011).

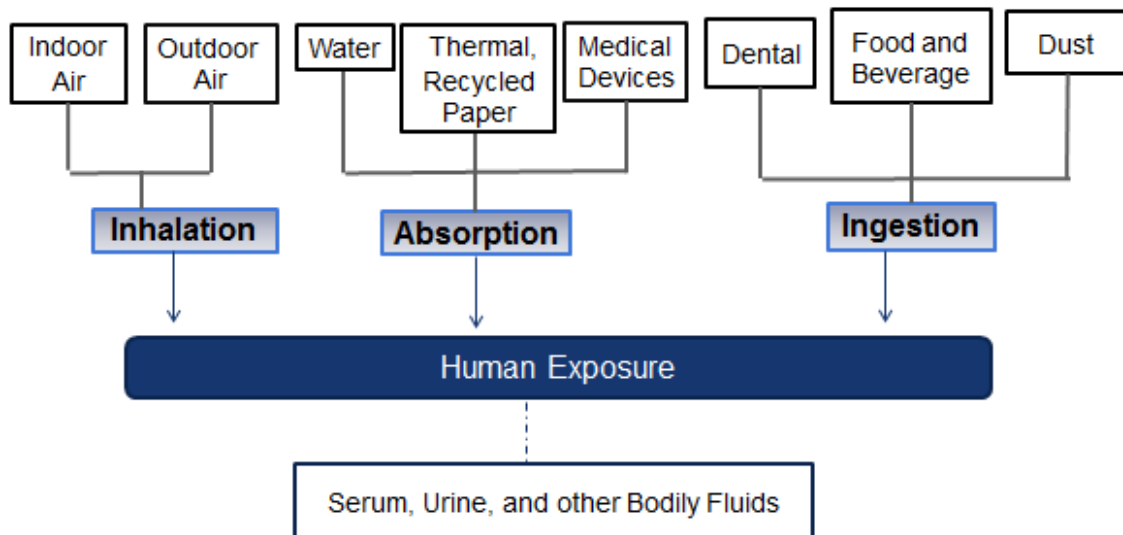
There are many compounds known to migrate into food, and the FDA sets a migration limit for these packaging components (Duffy et al. 2006). Of particular interest to school-aged children are endocrine disrupting chemicals (EDC) because their developing bodies are especially vulnerable to hormone disruption. Sometimes only

small changes in hormone activity during development can cause permanent effects (Welshons et al. 2003). Besides affecting reproductive organ development, environmental endocrine disruptors have been shown to influence adipogenesis and obesity (Grun and Blumberg 2009; Janesick and Blumberg 2011; Rubin et al. 2001; vom Saal et al. 2012). There are over 50 EDC's that have been approved for use in food packaging in the United States and the European Union (Muncke 2009). Amongst the EDC's of concern is bisphenol-A (BPA), a synthetic chemical used as a monomer base in manufacturing polycarbonate plastic and as a polymer link in epoxy resins. Residual BPA remains after polymerization, allowing this monomer to migrate into foods it contacts (Goodson et al. 2004; McNeal et al. 2000; Munguia-Lopez and Soto-Valdez 2001; Munguia-Lopez et al. 2005). Higher urinary concentrations of bisphenol-A in children 6-19 years old has been associated with a greater prevalence of obesity (Trasande et al. 2012). In the Center for the Evaluation of Risks to Human Reproduction of the National Toxicology Program's expert panel report, they express "some concern that exposure to Bisphenol A potentially causes neural and behavioral effects." There is also "minimal concern that exposure to Bisphenol A potentially causes accelerations in puberty" (NTP 2008). Lower-income children may be at a greater-risk for BPA exposure. In a recent study, an association was found showing that families with lower income, lower food security, and accessing emergency food assistance had higher urinary concentrations of BPA (Nelson et al. 2012).

Bisphenol-A can enter the food system through migration from polycarbonate plastic bottles, dishes, utensils, and storage containers, the epoxy lining of canned foods and beverages, (Biles et al. 1997b; Brede et al. 2003; Brotons et al. 1995; Goodson et al.

2004; Yang et al. 2011) and from BPA found in paperboard used in food containers (Liao and Kannan 2011; Ozaki et al. 2004). Another area of concern is polyvinyl chloride (PVC) plastic film, or stretch cling wrap, used for food storage. Studies have shown BPA leaching from plastic stretch films, into test water, acetic acid, and olive oil (Lopez-Cervantes and Paseiro-Losada 2003). BPA is an additive in food packaging PVC films and in PVC products to eliminate excess hydrochloric acid occurring during manufacturing (Cao et al. 2010).

Figure 5.1: Conceptual Model of BPA Exposure Pathways



In addition to food, BPA exposure in humans can occur from multiple other pathways, as shown in **Figure 5.1**. BPA can be measured in household dust, indoor and outdoor air (Wilson et al. 2003; Wilson et al. 2007), water (Lee et al. 2004; Sajiki and Yonekubo 2002), thermal receipts (Geens et al. 2012; Liao and Kannan 2011), recycled paper (Ozaki et al. 2004), from dental sealants (Joskow et al. 2006; Olea et al. 1996) and some medical devices (Calafat et al. 2009). The main BPA exposure pathway is from dietary ingestion, accounting for 99% of total exposure in preschoolers (Wilson et al.

2007) and 74 – 88% for children 6-12 years old (von Goetz et al. 2010). These exposures can then be detected throughout the human body including in serum, urine, saliva, breast milk, semen, amniotic fluid, and follicular fluid (Vandenberg et al 2007, 2010).

One area of food contamination from packaging that has not been well researched in the United States is school meals. Some research has been conducted in school meals in Japan, confirming the existence of BPA leaching into the food from food packaging and tableware (Miyamoto and Kotake 2006; Yamano et al. 2008). This is a worthwhile area of research since, in the U.S., nearly 34 million children eat lunches from the National School Lunch Program every school day. Over 22 million of those children, due to their family's income level, receive their lunch for free or at a reduced price (Food Research and Action Center 2010). School children also receive snacks in after-school and enrichment programs through the National School Lunch Program (USDA 2010). More than 12 million children ate breakfast through the School Breakfast Program every day in Fiscal Year 2011. Of these children, over 10.1 million of them received their meals free or at a reduced-price (USDA 2012). Research shows reason for concern about children's exposure to BPA from school meals. In a study of the National Health and Nutrition Examination Survey (NHANES) 2005-2006 Food Frequency Questionnaire data, higher urinary BPA concentrations were found to be associated with reported consumption of school lunches (Lakind and Naiman 2011).

In a risk assessment conducted by Miyamoto and Kotake, BPA exposure dose from school meals was modeled, aggregating dose pathways from food and serving materials. BPA migration was measured from school lunch polycarbonate (PC) tableware into food. It was assumed that a PC rice bowl, soup bowl, deep dish, a small dish, and

epoxy resin coated chopsticks were being used in all school meals. An encouraging finding in their study discovered that the use of PC tableware decreased after social concern for use of BPA in Japan was raised in 1998 (Miyamoto and Kotake 2006). In Yamano's research in schools, a 40.1% use of PC dishes in 1998 decreased to 10.2% in 2003. They discovered BPA in 32% of PC dishes from elution studies of the PC dishes. No BPA was detected in the substituted dishes. There has been a nationwide effort in Japan to substitute the use of PC dishes with polypropylene dishes. Also, since 2001, the inside of beverage containers has been substituted by cans that are lined with a polyethylene terephthalate (PET) film instead of epoxy resin in Japan. Yamano's laboratory was able to detect a significant drop in urinary BPA concentrations in its study subjects from before and after the effort to remove BPA from the system (Yamano et al. 2008).

The goal of this research is to model the potential exposure dose of bisphenol-A migrating from packaging into food served in a typical school meal. The meal is modeled after the food service of school that participates in the National School Lunch Program (NSLP) and School Breakfast Program (SBP). These daily doses will then be compared to the allowable dose of 50 $\mu\text{g/kg-BW/day}$ determined by the EPA to be a safe chronic exposure level for BPA.

Methods

The probabilistic and deterministic exposure models of potential bisphenol-A exposures from school meals were informed by formative research that used a mixed-methods approach including semi-structured interviews with stakeholders in food service, ongoing communication with key school food partners, a food service director survey, school kitchen and cafeteria visits, and a literature review for BPA food concentration values. Survey answers to the questions about the most popular school lunch, most popular school breakfast, and food contact materials were used to inform the exposure dose models. Details of the formative research informing the exposure models can be found described in a separate manuscript.

In order to calculate the potential amount of BPA children are exposed to from their school meals, exposure assessment techniques were employed. There are two ways to calculate exposure dose: from an aggregate method that estimates dose from all exposure pathways or with back calculations from a biomarker of dose. For this exposure assessment, a forward method is used to estimate aggregate BPA dietary exposures. The potential daily dose for BPA exposure from school meals was calculated from the exposure dose equation of:

$$\text{Daily Dose} = \frac{\sum_f (C \times IR)}{BW}$$

Σ_f = Sum of food items

C = BPA concentration

IR = Intake Rate

BW = Body Weight

The common back calculation method that starts with a known urinary BPA concentration used to estimate exposure was not utilized in this study (Miyamoto and Kotake 2006; NTP 2008).

The dose modeling equation first uses the BPA concentration of the food type multiplied by the intake rate of this food. All of the foods in a meal are then summed. Next, this sum is divided by body weight. After multiplying by a unit conversion factor, the resultant is the daily BPA dose measured in $\mu\text{g}/\text{kg-BW}/\text{day}$.

The meal components and quantity of food used for the model were guided by the new USDA guidelines for a reimbursable meal for schools that participate in the National School Lunch Program and School Breakfast Program. These latest guidelines are in compliance with the Child Nutrition Reauthorization Healthy, Hunger-Free Kids Act of 2010. Schools utilize the offer versus serve method, allowing students a choice in the foods they select. Each student is obligated to take each of the required food types or components to be considered a complete meal. **Table 5.1** is a simplified outline of the required components and the minimum daily portion size for a reimbursable school meal (Sodexo Training Module 2012).

Table 5.1: School Meal Components and Minimum Daily Serving Size

Meal	Meal Component	Minimum Daily Serving Size
Breakfast	Fruit	1 cup
	Grain	1 ounce
	Milk	1 cup
Lunch	Fruit	$\frac{1}{2}$ cup
	Vegetable	$\frac{3}{4}$ cup
	Grain	1 ounce
	Meat/Meat Alternative	1 ounce
	Fluid Milk	1 cup

Portion size differences by grade level are outlined in the National School Lunch Program and the School Breakfast Program. The minimum portion requirements for K-5 and 6-8 grades are the same and since the minimum required portion size per meal components were used in the scenarios, the same intake rate was used for all grades in the model. Grades 9-12 have a larger portion size minimum and maximum. High school grades were not modeled in these dose equations since observations in public high schools were not conducted in this research.

The body weights applied to this model are those recommended by EPA for use in risk assessment with default body weights varying by age category. The default weight used in the deterministic model for the K-5 students was 31.8 kg, the mean weight for the 6 to <11 years age category. For middle school grades 6-8, the default mean weight for 11 to <16 year olds of 56.8 kg was utilized for the deterministic model (EPA 2011). There was no differentiation in male and female students when applying the default weights. In the probabilistic model, the body weights were set to a normal distribution with set points for minimum and maximum weight and the 10th and 90th percentile weights. The 10th and 90th percentiles used values from the EPA (EPA 2011) and the minimum and maximum body weight values were derived from the EPA default weight source data, NHANES 1999-2006 (CDC 2012).

The main dishes selected for the model were the meals designated as the top sellers by the food service director survey administered in this research. The other components were chosen to represent the typical foods observed in the school site visits or informed from food service director interviews.

BPA concentrations per food type were chosen from published literature. Many studies have shown the migration of BPA from the can linings into its contents, either from directly measuring the contents of a can or through simulation studies. Only studies that analyzed the actual contents of the can were included. In most cases, the contents of the can were homogenized before analysis (Cao et al. 2010; Cao et al. 2011; Goodson et al. 2002; Imanaka et al. 2001; Sajiki et al. 2007; Schechter et al. 2010; Thomson and Grounds 2005). In cases where there were separate measurements of the solid and the liquid portion of the can contents, the BPA concentration values from the solid portion were used since this is the portion of the food that would be consumed (Noonan et al. 2011; Yoshida et al. 2001). Some published research also analyzed fresh food, food from plastic containers, and food from cardboard containers (Cao et al. 2011; Imanaka et al. 2001; Sajiki et al. 2007). These values were applied to BPA concentrations of milk, cereal, and for fresh fruits and vegetables in the exposure model.

The food's BPA concentrations were utilized in the deterministic and probabilistic calculations. For the deterministic calculations, the median BPA concentration values were used. For the probabilistic calculations, all available values were entered and were assumed to have equal probability of being selected for use in the model. If there were non-detectable concentrations of BPA reported in a paper, the value entered into the model was the limit of detection (LOD) divided by the $\sqrt{2}$. This method is recognized as being appropriate for exposure assessment when values are below the limit of detection (Hornung and Reed 1990). It is preferred that this method is not used when more than half of the values are below the limit of detection, as was the case for canned peaches and milk. Despite this, the method of $\text{LOD}/\sqrt{2}$ was applied to the below LOD values for

canned peaches and milk to provide comparability with the other foods in the model.

Table 5.2 displays the BPA concentrations and their sources for foods utilized in the exposure models.

Table 5.2: BPA Concentrations in Foods used in Exposure Dose Models

Meal Component	Food/ Ingredient	BPA Concentration Values (ng/g)	Study	Country of Study	Notes about study
Lunch Main Dish <i>Pizza</i> Grain Meat/Meat alternative	cheese	2.24	Cao et al 2011	Canada	
	canned tomato paste	<20	Schechter et al	United States	
	canned tomato paste	<0.6, 0.79, 0.82, 1.1, 1.3, 2.1	Cao et al 2010	Canada	
	canned tomato paste	86	Imanaka et al	Japan	
	flour	0.44	Cao et al 2011	Canada	
	yeast	8.52	Cao et al 2011	Canada	
Breakfast Main Dish	cold cereal	1, 3, 4, 14	Sajiki et al	Japan	used by von Goetz, packaged in plastic
Vegetable	canned corn	5, 3, 20	Sajiki et al	Japan	
	canned corn	12, 14, 20, <10	Thomson and Grounds	New Zealand	
	canned corn	0.78, 0.54, 0.37	Schechter et al	United States	
	canned corn	18.4, 28.0, 52.5, 56.4, 57.4, 95.3	Yoshida et al	Japan	only solid portion analyzed for these values
	canned corn	6.5, 12, 2.3, 54, 9.3, 57, 52, 75, 39	Imanaka et al	Japan	
	canned corn	76, 4.2, 25	Noonan et al	United States	only solid portion analyzed for these values
	canned corn	16	Goodson et al	United Kingdom	
	lettuce	<0.2	Cao et al 2011	Canada	
	carrots	<0.2	Cao et al 2011	Canada	
Fruit	canned peaches	<0.2	Sajiki et al	Japan	
	canned peaches	<10, <10, <10, <10	Thomson and Grounds	New Zealand	
	canned peaches	<10	Yoshida et al	Japan	only solid portion analyzed for this value
	canned peaches	9.3, <2, 6.3, 7.0, <2	Noonan et al	United States	only solid portion analyzed for this value
	raisins	0.51	Cao et al 2011	Canada	
	apple slices	<0.2	Cao et al 2011	Canada	
Fluid Milk	cow's milk	< 0.2, <0.2	Sajiki et al	Japan	
	cow's milk	< 0.5	Imanaka et al	Japan	
	cow's milk	<0.2	Cao et al 2011	Canada	

The exposure scenarios included low, moderate, and high potential exposures for breakfast and lunch for children in kindergarten to eighth grade. The term “high exposure” was applied to scenarios where a majority of food components were canned or packaged in plastic. A “moderate exposure” included a balance of packaged food and fresh foods in the meal. A “low exposure” scenario included a minimal amount of canned or plastic packaged food in the meal. Details of which foods and the quantities included in each meal and exposure scenario are included in **Table 5.3**.

Table 5.3: Exposure Scenarios

<i>Meal</i>	<i>Potential BPA Exposure</i>	<i>Grade Level Range</i>		<i>Foods</i>	<i>Intake Rate¹</i>
Breakfast	High	K to 5	6 to 8	Cold Cereal packaged in plastic	21.26 grams
				Milk	1 cup
				Canned Peaches	1 cup
	Moderate	K to 5	6 to 8	Cold Cereal packaged in plastic	21.26 grams
				Milk	1 cup
				Raisins	1.5 ounces
				Canned Peaches	1/2 cup
	Low	K to 5	6 to 8	Cold Cereal packaged in plastic	21.26 grams ²
				Milk	1 cup
				Sliced apples	1 cup
Lunch	High	K to 5	6 to 8	Cheese pizza	1 slice ³
				Canned Corn	3/4 cup
				Canned Peaches	1/2 cup
				Milk	1 cup
	Moderate	K to 5	6 to 8	Cheese pizza	1 slice
				Canned corn	1/4 cup
				Lettuce	1 cup ⁴
				Canned Peaches	1/2 cup
				Milk	1 cup
	Low	K to 5	6 to 8	Cheese pizza	1 slice
				Lettuce	1 cup
				Raw Carrots	1/4 cup
				Sliced apples	1/2 cup
				Milk	1 cup

¹ Intake rate calculated with 100% consumption of food served and with the average plate waste of 12%

² Intake rate is the median value of the 5 kinds of individually packaged cereal bowls observed

³ 1 serving of cheese pizza based on USDA recipe; BPA concentrations based on the ingredients of cheese, flour, yeast, tomato paste

⁴ 1 cup lettuce is equivalent to 1/2 cup serving of vegetable according to the NSLP

Frequently, some portion of a school meal goes uneaten, leading to plate waste. The plate waste has been studied and reports show that an average of 12% of calories from a school meal are not consumed ((Buzby and Guthrie 2002). To account for this phenomenon, for each meal and dose scenario level, intake rate was calculated for 100% of the food served was eaten and also calculated with the average plate waste, when 12% of the calories were left uneaten. To account for plate waste, the exposure dose calculation reduced the intake rate by 12% of its calories. The equation used for modeling plate waste exposure doses is:

$$\text{Daily Dose} = \frac{\sum_f [C \times (IR \times PW)]}{BW}$$

Σ_f = Sum of food items

C = BPA concentration

IR = Intake Rate

BW = Body Weight

PW = Plate Waste

All twelve exposure dose scenarios were modeled with a single, deterministic calculation, and then with probabilistic calculations using Crystal Ball software (Oracle USA, Inc., Redwood City, CA). The probabilistic models were run with 1000 simulations each, set to use Monte Carlo sampling methods to allow the whole range of

values to be chosen randomly. Each value of the distributions was set to be sampled with equal probability. **Table 5.4** summarizes the parameters for the exposure models.

Table 5.4 Parameters of BPA Exposure Modeling of School Meals

Parameter	Values and Units	Distribution Form	Data Source(s)
Intake Rate	ng; See Table 5.3 for values	Point Values	National School Lunch Program and School Breakfast Program portion requirements, from observed package sizes
BPA Concentration of Foods	ng/g; See Table 5.2 for values	Point Values	See Table 5.2 for sources
Body Weight	<div> <div>K-5th grade: min 14.5 kg, 10th 21.3 kg, 50th 31.8 kg, 90th 45.6kg, max 89 kg</div> <div>6th-8th grade: min 20.4 kg, 10th 37.2 kg, 50th 56.8 kg, 90th 79.3 kg, max 181.3 kg</div> </div>	Normal Distribution using EPA recommended default weights for 50th percentile, and actual min, max, 10th, 90th percentiles from the NHANES 1999-2006 data	EPA Exposure Factors Handbook 2011 Tables 8.1, 8.3 with values based on NHANES 1999-2006; minimum and maximum data from NHANES 1999-2006 datasets
Plate Waste	12% of total calories	Point Values calculated for each exposure scenario	Buzby and Guthrie 2002

Results

The potential BPA exposure doses forecasted by the simulation models, as displayed in **Tables 5.5** and **5.6**, had a broad range of values. The potential doses ranged from 7.7×10^{-4} µg/kg-BW/day for the minimum low exposure breakfast for a 6th - 8th grader with average plate waste to a high of 0.97 µg/ kg-BW/day for the maximum high potential exposure meal consumed during lunch for a K-5 student. These two values were calculated from the probabilistic models.

Table 5.5: Deterministic and Probabilistic BPA Exposure Doses for K to 5th Grade

BREAKFAST Dose (µg/kg-BW/day)by Exposure Scenario						
Model Type Percentiles	Low	Low Plate Waste	Moderate	Moderate Plate Waste	High	High Plate Waste
Deterministic	0.0044	0.0038	0.029	0.026	0.054	0.047
Probabilistic:						
Minimum	0.0013	0.0015	0.0048	0.004	0.0066	0.0062
5%	0.0023	0.002	0.0079	0.0068	0.011	0.0095
25%	0.0033	0.003	0.021	0.017	0.036	0.031
50%	0.0045	0.004	0.028	0.024	0.048	0.042
75%	0.0075	0.0069	0.035	0.03	0.063	0.054
95%	0.014	0.013	0.049	0.044	0.09	0.076
Maximum	0.026	0.022	0.076	0.071	0.15	0.13
LUNCH Dose (µg/kg-BW/day) by Exposure Scenario						
Model Type Percentiles	Low	Low Plate Waste	Medium	Medium Plate Waste	High	High Plate Waste
Deterministic	0.0074	0.0076	0.06	0.054	0.17	0.1
Probabilistic:						
Minimum	0.0039	0.0039	0.0057	0.0067	0.0073	0.0049
5%	0.0051	0.0051	0.017	0.018	0.025	0.022
25%	0.0067	0.0064	0.039	0.034	0.057	0.05
50%	0.0084	0.0083	0.062	0.054	0.1	0.098
75%	0.012	0.011	0.11	0.092	0.24	0.22
95%	0.052	0.047	0.19	0.17	0.48	0.41
Maximum	0.11	0.092	0.45	0.36	0.97	0.83

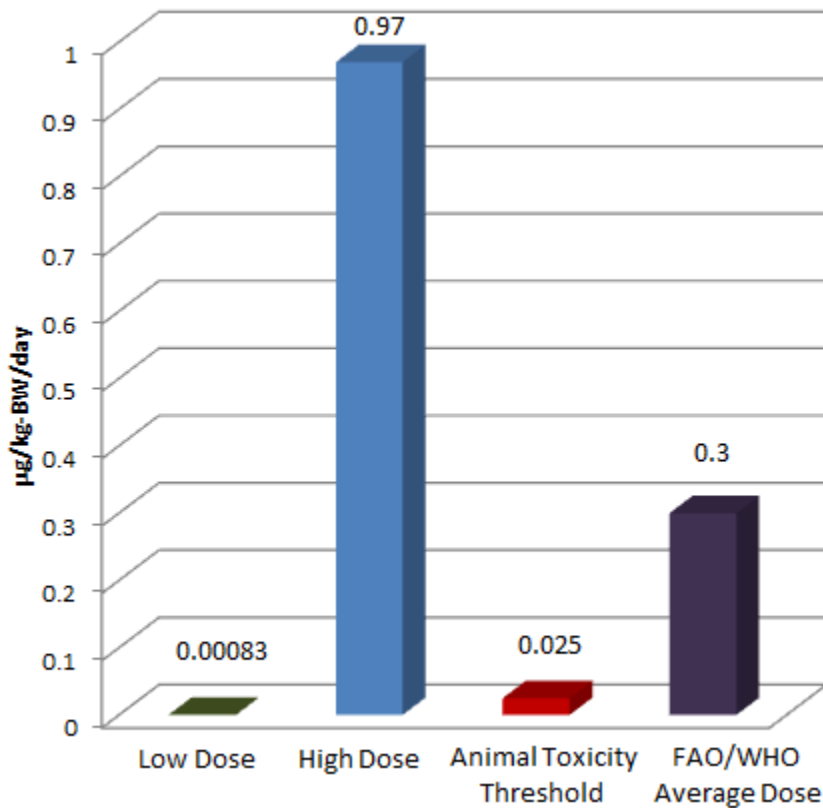
Table 5.6: Deterministic and Probabilistic BPA Exposure Doses for 6th to 8th Graders

BREAKFAST Dose (µg/kg-BW/day)						
Model Type Percentiles	Low	Low Plate Waste	Moderate	Moderate Plate Waste	High	High Plate Waste
Deterministic	0.0024	0.0021	0.016	0.014	0.03	0.026
Probabilistic:						
Minimum	0.00083	0.000772	0.0026	0.0019	0.0041	0.0032
5%	0.0012	0.0011	0.0045	0.004	0.0065	0.0054
25%	0.0019	0.0017	0.012	0.01	0.021	0.018
50%	0.0025	0.0023	0.016	0.014	0.029	0.024
75%	0.0046	0.0041	0.02	0.018	0.037	0.032
95%	0.0083	0.0074	0.031	0.027	0.055	0.049
Maximum	0.016	0.015	0.054	0.06	0.088	0.08
LUNCH Dose (µg/kg-BW/day)						
Model Type Percentiles	Low	Low Plate Waste	Moderate	Moderate Plate Waste	High	High Plate Waste
Deterministic	0.0042	0.003	0.034	0.03	0.065	0.058
Probabilistic:						
Minimum	0.0022	0.0014	0.0023	0.0034	0.0039	0.0038
5%	0.0029	0.0021	0.0099	0.0099	0.015	0.013
25%	0.0038	0.0027	0.022	0.019	0.033	0.028
50%	0.005	0.0035	0.035	0.031	0.059	0.057
75%	0.0075	0.0053	0.061	0.054	0.14	0.13
95%	0.029	0.024	0.11	0.096	0.28	0.25
Maximum	0.057	0.06	0.22	0.19	0.64	0.58

The values modeled are 50 to 10,000 times lower than the EPA Oral Reference Dose (RfD) of 50 µg/kg-BW/day. The highest modeled dose of 0.97 µg/kg-BW/day is approximately 50 times lower than the RfD. **Figure 5.2** compares this research's low dose and high dose are compared with the threshold for animal toxicity of 0.025 µg/kg-BW/day (vom Saal and Hughes 2005) and the FAO/WHO's estimated average daily BPA exposure for children and teenagers, derived from the range of 0.1 to 0.5 µg/kg-BW/day

(FAO/WHO 2010). This figure illustrates how many doses modeled are above the animal toxicity threshold and the average daily exposures estimated in other research.

Figure 5.2: Modeled BPA Doses Compared with Toxicity and Population Dose Estimates



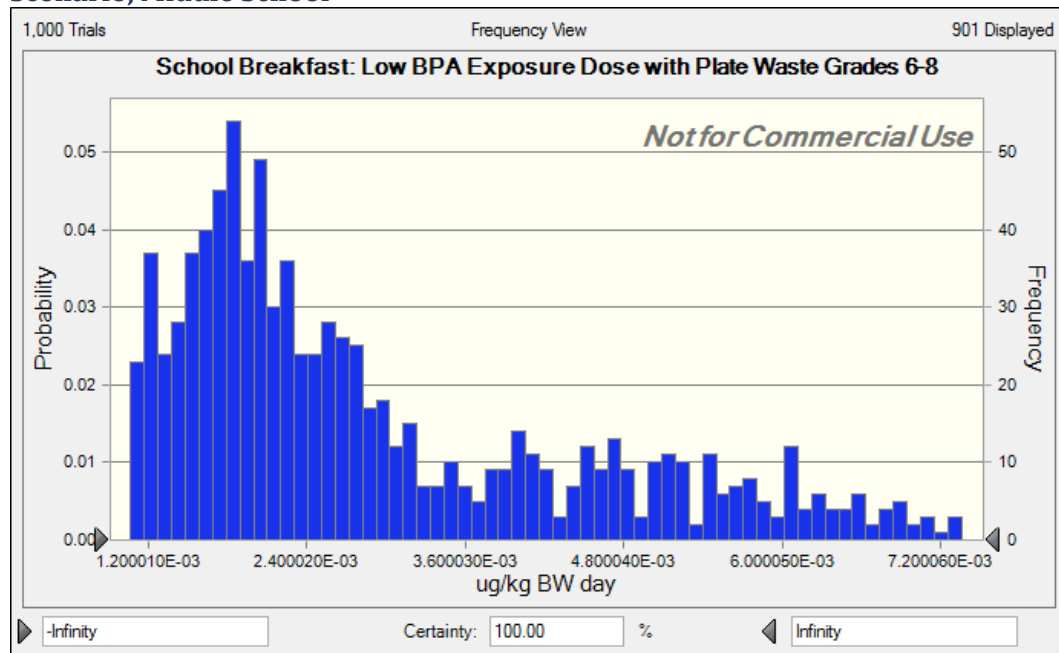
Deterministic calculations were similar in value to the median values calculated in the probabilistic model. The deterministic range of values from breakfast was 2.14×10^{-3} µg/kg-BW/day to 5.38×10^{-2} µg/kg-BW/day. The range of values for lunch was 3.05×10^{-3} µg/kg-BW/day to 1.17×10^{-1} µg/kg-BW/day. For both meals, the deterministic low doses were between the 25th and 50th percentile in the probabilistic models. For the moderate and high breakfast doses, the deterministic model was between the 50th and 75th percentiles for the probabilistic models. For lunch, the deterministic calculation wavered

between the 25th and 50th percentile of probabilistic calculations for some models and the 50th and 75th percentile for others.

In the probabilistic models, sensitivity analysis showed that the most influential food exposure component in the models varied with the exposure levels. For a low exposure breakfast, cereal was the driving force, determining 77-80 % of the forecasted exposure dose. For the moderate and high exposure breakfast, canned peaches were the driving force, determining 55-68 % of the exposure estimate. During lunch, the most influential BPA concentration is tomato paste for the low exposure calculations, accounting for 56-63 % of the forecasted exposure. For the moderate and high exposure models, canned corn is the main factor in the dose, accounting for 78-93 % of the dose estimate.

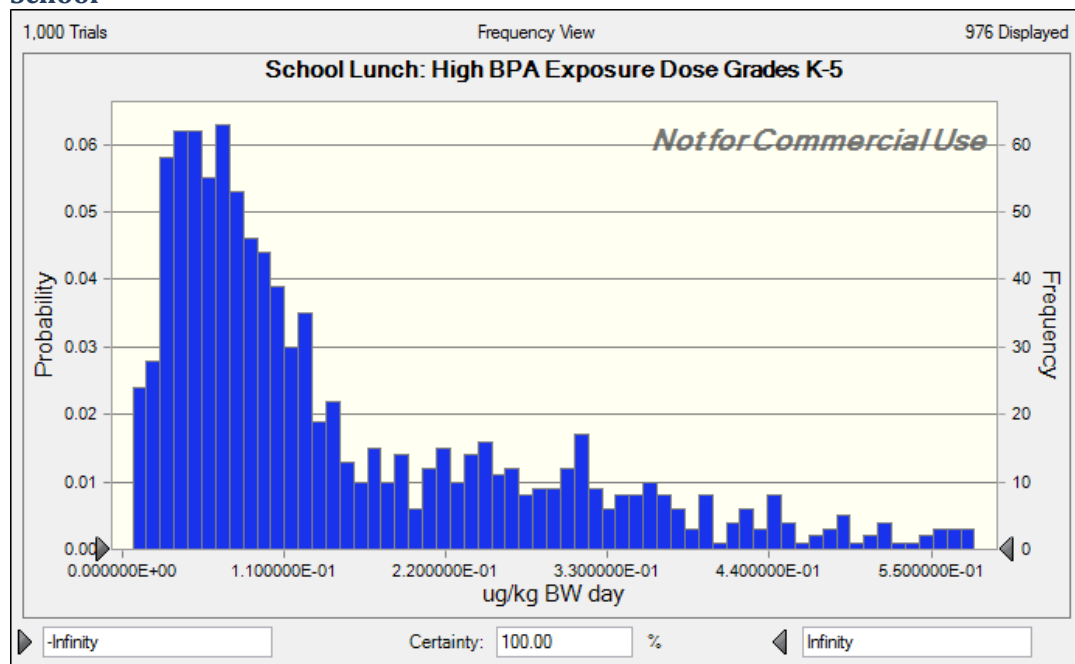
The frequency distribution for probabilistic modeling of the lowest doses calculated is displayed in **Figure 5.3**. This is the exposure estimate forecast for a low BPA exposure breakfast for middle school children with average plate waste.

Figure 5.3: Frequency Distribution for Breakfast Low Exposure with Plate Waste Scenario, Middle School



The frequency distribution for the highest exposure dose estimates, lunch with high exposure for grades K-5, is displayed in **Figure 5.4**.

Figure 5.4: Frequency Distribution for Lunch High Exposure Scenario, Elementary School



Discussion

This study successfully integrated multiple data collection methods to inform the BPA exposure dose models. Input values for the models included data points assembled from formative research efforts that included school meal service personnel interviews, a food service director survey, school site visits, government guidance documents, and scientific journals. This study was the first known probabilistic modeling of BPA in school meals in the United States.

Daily doses derived in this study are the same magnitude as other studies modeling aggregate BPA exposures from food sources. To compare to our modeled doses of 7.7×10^{-4} $\mu\text{g/kg-BW/day}$ to $0.97 \mu\text{g/kg-BW/day}$, Miyamoto and Kotake modeled children ages 7 to 14 years old being exposed to an average of $0.55 \mu\text{g/kg-BW/day}$ (Miyamoto and Kotake 2006). Imanaka's duplicate diet studies of adults modeled their doses in the range of 0.004 to $0.11 \mu\text{g/kg-BW/day}$ (Imanaka 2001; Ministry of the Environment of Japan 2003). For total diet studies from Tokyo, 2-6 year olds were modeled with a dose of $0.00475 \mu\text{g/kg-BW/day}$ and adults with a dose of $0.00195 \mu\text{g/kg-BW/day}$ (Tokyo Metropolitan Government 2003). In von Goetz's BPA exposure assessment, the aggregate daily dose for a child from food is $0.0267 \mu\text{g/kg-BW/day}$ for a mean exposure scenario and $0.0164 \mu\text{g/kg-BW/day}$ for a high exposure scenario (von Goetz et al. 2010).

Although the highest modeled dose of $0.97 \mu\text{g/kg-BW/day}$ is approximately 50 times lower than the RfD, it is above the threshold for animal toxicity of $0.025 \mu\text{g/kg-BW/day}$ from more recent research. Many of the doses modeled in this research exceed

this toxicity threshold value, illustrating the potential for school meals to place children at risk for toxic exposures from BPA. Low dose animal toxicity studies of BPA have spurred scientific debate about the relevance of the current reference dose. The current BPA reference dose is determined from a 1000 fold uncertainty factor applied to the LOAEL of 50 mg/kg-BW/day. The LOAEL is based on the adverse health effect of weight loss observed in rodents fed oral doses of BPA, a high-dose toxicity study conducted by NTP in 1982 (US EPA IRIS 2012). The validity of continuing to use this study as the basis of a reference dose in light of more recent research findings has been called into question. Since the time the RfD was established in 1988, there have been over a hundred papers published on the subject of low dose animal studies of BPA exposure. When one compares the findings of these studies to the LOAEL, most of these newer animal studies show adverse health effects at exposures 10,000 times lower than the current LOAEL. Animal toxicity studies showed adverse health effects as much as 1,000,000 times lower than the LOAEL, at 0.025 µg/kg-BW/day (vom Saal and Hughes 2005).

Another concern of using the current BPA RfD is that endocrine disrupting chemicals can display non-monotonic dose response curves (NMDRC). NMDRCs are non-linear and have slopes that change signs within the range of tested doses. A NMDRC may display a curve shaped like a U, an inverted U, or a multiphasic curve where response increases and decreases multiple times as the dose increases. The typical extrapolation process of low-dose response from high-dose response points, as was used to establish the BPA RfD, cannot be applied to a NMDRC. NMDRCs raise concern over the use of high dose toxicity studies as basis for establishing safe exposure levels for

endocrine disrupting chemicals, as is currently used for BPA's RfD (Vandenberg et al. 2012). As more is learned about endocrine disrupting chemicals, there is evidence showing BPA's ability to incite reproductive effects through multiple mechanisms of action. In contrast, some scientists support traditional toxicological methods evaluating BPA toxicity through a single mechanism of action, the modulation of the (nuclear) estrogen receptor (Gray et al. 2004). As a result, there are differing opinions on how BPA risk should be assessed.

There are some limitations to this exposure modeling study. First, not all of the potential BPA exposure pathways were accounted for in the exposure model. This study focused on dietary exposures and did not account for BPA exposures from the air, water, dust, dental, or medical products. As for dietary exposures, only foods with published BPA concentrations could be included. These foods are almost exclusively canned foods, with some other foods that are processed or packaged in plastic. The omission of these potential sources of BPA exposure likely resulted in an underestimate of BPA exposure in the models.

A second shortcoming is that the BPA concentrations for food used in the model were selected from multiple studies, many of which were conducted outside of the U.S. Most of the BPA values were from North American studies: selecting data from Cao's work in Canada, and Noonan and Schecter's works in the U.S. (Cao et al. 2010; Cao et al. 2011; Noonan et al. 2011; Schecter et al. 2010). The North American research would most likely represent the food sources that U.S. children would be exposed. Other studies were conducted in Japan, New Zealand, and the United Kingdom (Goodson et al. 2002; Imanaka et al. 2001; Sajiki et al. 2007; Thomson and Grounds 2005; Yoshida et al.

2001). Selecting research from North America does not guarantee that the BPA concentrations found in those studies will represent the BPA concentration that would be found in the foods in a person's local supermarket. Noonan's research has shown that there is great variation in the lining of cans, and therefore the BPA content, between can manufacturers. Even the same type of food from the same brand may be packaged in cans from different can manufacturers (Noonan et al. 2011). Can manufacturers are protected by trade secret rights making the confirmation of exact formulations challenging for researchers.

Another limitation of the exposure modeling was that for some foods there was only one published BPA concentration value. In these cases, the BPA exposure for that food became a deterministic calculation with this segment of the model remaining static. It was decided to include foods with limited data than to cause more inaccuracy by eliminating these single data points from the study.

The canned food analyzed for the BPA concentrations used in this modeling exercise were purchased from the grocery store in sizes meant for household level use. These cans are in the range of 10 – 16 ounces. Canned goods used in schools are much larger, institutional size cans, also called a number 10, which usually hold 6.5 to 7.5 pounds. There is potential that the BPA concentrations of food packaged in institutional sized cans may actually be less since there is less surface area for food to be exposed to. Unfortunately, no research has analyzed food from these larger cans to confirm these assumptions.

A newer facet to the BPA debate is the extent of BPA contamination of paper and paper products. Most of the schools visited in this research served their food in single-use

paperboard dishes. In addition to the known migration of BPA from polycarbonate dishes and epoxy lined cans, emerging research expresses a concern over the BPA content of paper and paper products. Ozaki discovered that 0.034-0.36 $\mu\text{g/g}$ can be found in food packaging paperboard from virgin materials. Food packaging paperboard from recycled materials can have ten times more BPA, at 0.19-26 $\mu\text{g/g}$ (Ozaki et al. 2004). There has additionally been a study from Spain testing the papers and paperboard boxes from take-away restaurants. This application is very similar to a cafeteria environment where there is minimal time between the cooking of the food, its placement in a wrapper or container, and consumption. In this study, 90% of the food contact papers and boxes had detectable levels of estrogenicity and 48% had detectable levels of BPA (Lopez-Espinosa et al. 2007). In the site visits conducted for this research, it was observed that many schools serve food directly on disposable paperboard trays. The amount of BPA that children may be exposed to from this pathway could not be accounted for in this model because no migration exposure studies about food contact from paperboard are available in published literature. There are related studies on dermal BPA exposure from paper sources in the literature. BPA exposure from multiple paper products, such as thermal receipts, tickets, magazines, newspapers, and business cards were used to calculate a daily dose of 0.219 ng/kg-BW/day for an 80 kg adult. Ninety-nine percent of this dose is attributed to handling of receipts, an activity atypical for schoolchildren. The exposure model's other sources such as paper napkins, paper towels, and toilet paper exposure would contribute to a child's daily exposure (Liao and Kannan 2011). These data show that more research on migration of BPA from paper food containers into school food is warranted.

Dust and soil ingestion and air inhalation pathways were not included in this exposure model and are known to be only minor contributors to BPA exposure in comparison to food contributions (Kang et al. 2006; von Goetz et al. 2010; Wilson et al. 2007). Some figures are available to make aggregate estimates. FAO/WHO information estimates BPA exposure from inhalation is 0.003 $\mu\text{g/kg-BW/day}$ for the general population and 0.0001 to 0.03 $\mu\text{g/kg-BW/day}$ from soil or dust ingestion for the general population and infants, respectively (FAO/WHO 2010). In von Goetz's aggregate BPA exposure modeling exercise, the 2.5 ng/kg-BW/day figure for a child's mean exposure scenario daily house dust dose was used (von Goetz et al 2010, originally from Mattalut et al, but this article is only available in German). BPA exposure from air is estimated as 0.9 ng/kg-BW/day for a child's mean exposure scenario. These figures are from air monitoring in a daycare setting (Wilson et al. 2007). If one adds the exposure doses for air, dust/soil, and paper products to the moderate exposure scenario for lunch of $6.04 \times 10^{-2} \mu\text{g/kg-BW/day}$, the doses using the FAO/WHO figures result in $6.46 \times 10^{-2} \mu\text{g/kg-BW/day}$ and $6.76 \times 10^{-2} \mu\text{g/kg-BW/day}$ utilizing von Goetz's figures. Although the addition of air, dust, and soil exposures do not increase the magnitude of the exposure values, it is worthwhile to continue to understand BPA exposures from non-dietary sources for a better overall picture of BPA exposure contributions.

Conclusions

Using data points from the formative research, this study provides valuable insight into the potential BPA exposures from school meals. The food service director survey and school site observations showed that school meal components largely come to schools in plastic bags, are served onto plastic trays, and eaten with plastic utensils. Although not all of these potential BPA exposure pathways were accounted for in the exposure model due to a lack of available data, from the sources that could be modeled this study forecasted BPA exposure from school meals to be from 7.7×10^{-9} $\mu\text{g/kg-BW/day}$ to $0.97 \mu\text{g/kg-BW/day}$. These numbers are low compared to the reference dose of $50 \mu\text{g/kg-BW/day}$.

Future research on school meal BPA exposures should investigate the BPA content of the unique foods served in schools. The published studies reviewed in this research effort found that lab studies almost exclusively purchased their foods from supermarkets in an effort to emulate foods typically eaten at home. Some studies have also looked at fast foods (Cao et al. 2011). The only institutionally based studies were Japanese studies evaluating BPA in schools (Miyamoto and Kotake 2006; Yamano et al. 2008) and one that studied hospital food (Imanaka 2001). Institutional food preparation is unique because it utilizes larger sized canned goods, uses bulk pre-cooked proteins, bulk pre-prepared meals, and also utilizes many individually packaged foods. Analysis of this pattern of food service is a valuable endeavor.

To better estimate BPA exposures in school meals and other institutional settings, future laboratory studies should fill in the gaps about BPA food contact exposure from foods that have contact with paperboard serving trays and from use of paper napkins.

They should also be looking at the other sources of food contact such as the plastic utensils and plastic serving trays used in almost all school cafeterias.

Further research should take a holistic look at the food intake of low income children. Besides their potential exposure to foods from the School Breakfast Program and the National School Lunch program, these children may be from families receiving food assistance. Food bank food could be more highly packaged due to the need for non-perishable food sources. This could lead to a greater exposure of low-income children to foods stored in packaging that contains BPA or other endocrine disrupting chemicals.

Although focus of this study was directed at BPA exposures, there needs to be a broader focus on all of the chemicals and indirect additives from packaging, be it from paper or plastic. A growing body of research shows the many sources of endocrine disrupting chemicals migrating into food (Duffy et al. 2006; Lopez-Cervantes and Paseiro-Losada 2003; Lopez-Espinosa et al. 2007; McNeal et al. 2000; Muncke 2009; Ozaki et al. 2004). Additional evidence of low-dose and NMDRC for endocrine disrupting chemicals has elevated the debate about the ability to continue use of high dose toxicity testing as the basis for establishing safe doses for this class of chemicals. On a promising note, regulatory agencies are examining their current scientific opinion and regulatory frameworks governing endocrine disrupting chemicals. In 2012, both the EFSA and the EPA have formed special task forces to review the science and decision-making processes regarding this issue (EFSA 2012b; Environmental Health News 2012). This action confirms the need to magnify research efforts towards this class of chemicals that can disproportionately affect the youngest and most vulnerable in our population.

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CHAPTER SIX: Policy and Advocacy Directions to Reduce BPA Exposures

Introduction

Bisphenol-A (BPA), is an endocrine disrupting chemical (EDC) commonly found in consumer products (Tsai 2006), medical devices (Calafat et al. 2009), dental sealants (Joskow et al. 2006; Olea et al. 1996), paper products (Geens et al. 2012; Liao and Kannan 2011) and food packaging materials (McNeal et al. 2000). Although BPA has demonstrated developmental and reproductive toxicity in animal testing, its health effects in humans are still under debate. It can readily leach into foods from polycarbonate plastic food vessels, epoxy resin lined canned food and beverages, and PVC food packaging materials, making the dietary intake the main source of BPA exposure. A salient goal for the federal government in the field of endocrine disruption is to establish regulatory frameworks and risk management strategies that can protect human health and the environment from overexposure to BPA and endocrine disrupting chemicals. The FDA and the EPA, the two agencies of the U.S. government in charge of protecting health and the environment with regard to BPA, have been stagnating on their decision-making. Their current opinion is that the science is uncertain and does not provide definitive proof of the connections between endocrine disrupting chemical exposures and negative health effects at low concentrations. Instead of advancing the regulatory frameworks to better deal with EDCs, the traditional paradigms of high dose toxicity testing and linear dose response are still guiding decisions.

The following policy perspective provides recommendations of how exposures to endocrine disrupting chemicals could be reduced through improved protections of

workers and other vulnerable populations, food contact materials regulations, consumers and advocacy group actions, and governmental policy reform. The policy analysis was prepared with the knowledge that the current science supporting low dose effect is imperfect and incomplete. It aims to balance actions that can be achieved within the current framework as well as policies developed to re-design the regulatory structure to meet the needs of endocrine disrupting chemicals.

Food Contact Materials Monitoring and Regulatory Reform for Endocrine Disrupting Chemicals

The first policy reform needed for the Food and Drug Administration (FDA), the agency in charge of regulating food contact materials, is to increase the availability of data from BPA migration studies of food. This action would improve the ability to characterize BPA exposure. The use of endocrine disrupting chemicals in food packaging and its migration into food is well known. Over 50 endocrine disrupting chemicals are approved for use in food packaging in the United States and the European Union (Muncke 2009). FDA laboratory studies acknowledge “suspected endocrine disruptors are present as additives or residues in food-contact materials” and “can be expected to migrate to some foods in very low amounts. Larger amounts of migration can be expected from polymers exposed to food at elevated temperatures, i.e., heat-processed foods” (McNeal et al. 2000). These “elevated temperatures” are exactly the treatment canned foods undergo during the sterilization process. Due to this knowledge, the migration of chemicals and elements from food packaging is being monitored in the United States by FDA laboratories. Research from these labs have shown the presence of endocrine disruptors in cheese, infant formula, PC water carboys, canned food, apple juice, and plastic film food wrapping. These foods were analyzed as part of the Total Diet Study (TDS) that monitors food contaminants for the most commonly consumed foods in America. The TDS measures foods for contaminants, seeking concentrations of pesticides, industrial chemicals, radionuclides, and toxic and nutrient elements. This research is conducted four times a year in each of the four geographic regions of the United States (FDA 2009; McNeal et al. 2000).

Although the testing for EDCs in food is reported to be frequent, the publication of this literature is scant. Publicly available FDA BPA exposure assessments are limited to two studies on BPA in infant formula (Ackerman et al. 2010; Biles et al. 1997a), two studies on BPA in canned and packaged food (McNeal et al. 2000; Noonan et al. 2011), and one study on BPA migration from polycarbonate food containers (Biles et al. 1997b). Upon examination of the Total Diet Study web-site, BPA is not listed as one of the packaging contaminants regularly monitored by the FDA, making it possible that BPA is not included in their regular monitoring protocol. BPA should be a TDS study chemical and the findings of the FDA's research should be made publicly available.

An additional issue with how endocrine disrupting chemicals in food contact applications are monitored is that the trigger points for toxicity testing may not be properly set at levels that would capture low dose toxicity for EDCs. In the U.S., reproductive toxicity testing is required for intentionally added substances when food simulants testing show leaching of 1 ppm, or 1mg/kg food or higher. These test points are below doses that have been shown to cause health effects in animal studies (Muncke 2011). As additional low dose animal studies show adverse health effects, there needs to be adjustments to the food contact materials regulations. The regulation trigger points need to be set at levels relevant to points of departure for endocrine disrupting chemicals. Without change, there is a risk of food contact materials being deemed safe by the FDA only because the criteria for recognizing safety have been improperly set.

The current food contact materials regulations focus on mutagenicity and genotoxicity testing. This narrow scope fails to examine endocrine disruption, developmental toxicity including obesogenicity, and the toxicity of mixtures. The

inadequate investigation of reproductive toxicity results in the weakened protection for women of childbearing age and pregnant women who are more sensitive to these types of exposures. Another vulnerable population is overweight and obese persons whose bodies' ability to metabolize xenobiotics has been altered (Muncke 2011). There is evidence that environmental endocrine disruptors may be influencing adipogenesis and obesity (Grun and Blumberg 2009; Janesick and Blumberg 2011; Rubin et al. 2001; Vom Saal et al. 2012). Monitoring for single compounds has the danger of missing endocrine disrupting activity. It is known that humans have many environmental estrogenic compounds in their body at one time (Vandenberg et al. 2007).

The current food contact materials regulations apply only to newly approved foods. The food contact materials legislation for previously approved materials, such as BPA, does not need to adhere to the stricter rules for food contact materials. An essential action to ensure that the safety of the food system is maintained is to bring the previously approved chemicals up to current standards. It is time to change food contact material regulations to allow the FDA to more closely regulate chemicals that were approved before the current regulations.

Testing for estrogen activity in materials needs to be consistent and accurate. In a study of 455 plastic food containers including ones labeled as BPA-free, estrogenic activity was detected in all of the products. This experience taught the researchers that the use of only one kind of solvent, as performed by many laboratories, will likely mischaracterize a substance as being estrogen activity-free. They recommend the use of both a more-polar and less-polar solvent for testing. Secondly, they believe that common

stress testing, such as microwaving, heating, and UV exposure of the test materials will allow for more accurate diagnosis of estrogenic activity (Yang et al. 2011).

In BPA migration studies, there is limited monitoring of fresh foods that have shown detectable levels of BPA (Cao et al. 2011; Sajiki et al. 2007; Schecter et al. 2010; Vivacqua, et al. 2003). Some attribute the BPA discovered in food to the plastic packaging. In some instances, BPA in fresh food is believed to have originated from air, soil, or water contamination. Another possible avenue of contamination is from plastic products used during cultivation. Fresh strawberries in Japan have detectable levels of BPA, thought to be from the plastic sheeting used to cover the soil in the greenhouses to maintain soil temperature or possibly from the PVC panels the greenhouse is made from (Sajiki et al. 2007). There should be an effort to clearly monitor BPA in fresh foods and also to discover the source of the contamination. Without knowledge of the source of BPA, proper mitigation strategies cannot be identified.

The FDA's current stand on finding BPA free alternatives to canned food linings is that it "supports changes in food can linings and manufacturing to replace BPA or minimize BPA levels where the changes can be accomplished while still protecting food safety and quality" (FDA 2012c). In addition to supporting industry changes, BPA reduction in the food system could move forward more quickly if the government would fund studies on alternatives to epoxy resin can linings with BPA. There is a current effort by EPA's Design for the Environment partnership program where it is working with private industry to find safe alternatives to BPA in thermal receipts (EPA 2013a). The same type of effort should be enlisted for food contact materials such as epoxy can linings. A government and industry partnership would provide perspective to both sides

regarding the challenges of finding BPA can lining replacement and the food contact approval process. This partnership could also serve to educate the public on the complexity of this issue. There can be government incentives to create new products and to transition to the new ones once they have been tested and approved. The FDA should partner with the canning industry to disclose their performance data, showing which foods can/cannot be canned with alternative linings safely.

To find safe alternatives to current can linings, one place to start is by evaluating the PET laminate can linings that Japan has been using for over a decade now. The government should evaluate whether these new linings are safe according to U.S. food contact materials standards and viable for the U.S. food market. Caution must be exercised in transitioning to BPA alternative chemistries. Emerging research on BPS, the chemical commonly used to replace BPA in polycarbonate plastic products and thermal receipts, has discovered that this compound demonstrates acute toxicity and endocrine disrupting properties (Chen et al. 2002; Kitamura et al. 2005; Viñas and Watson 2013). In a recent study sampling people in the United States and in seven Asian countries, 81% of the test population had detectable urinary concentrations of BPA. BPS concentrations were an order of magnitude lower than BPA from the same urinary samples, except in Japan, where the use of BPS as an alternative to BPA is pervasive (Liao et al. 2012).

Protection for Non-Dietary BPA Exposures

Over six billion pounds of BPA is being produced every year (CDC 2009). Less than 5% of the BPA being produced is being used in food contact applications (EPA 2012a). The other 95% of the BPA produced is being utilized in non-food applications to make consumer products such as safety glasses, CD's, headlights and taillights, being put into epoxy paints, dental composites and sealants, intravenous medical tubing, and implanted plastic medical devices, to name a few. This translates to numerous workers potentially being exposed to BPA in their workplace on a chronic basis.

It additionally means that there is potential for massive amounts of waste to be generated from these consumer products. The EPA reports over one million pounds of BPA is being released into the environment every year (EPA 2012a). There may be even more than the EPA is aware of being dumped or leaked into the environment since there is not a full accounting of consumer products throughout their life-cycle. Some are being recycled by being melted down, possibly causing occupational harm in this manner. The products going into landfills could then be contaminating landfill leachate. The multitude of uses of BPA and different manners of disposal have resulted in the detection of BPA in samples of the indoor and outdoor air, dust, soil, landfill leachate, and wastewater effluent (Tsai 2006; Vandenberg et al. 2007; vom Saal et al. 2007; Wilson et al. 2007). Moreover, it is incorporated into paper and paper products when thermal receipts are introduced into the recycling stream (Ozaki et al. 2004).

All of these numerous non-food BPA exposure sources are considered to be the minor exposure pathways of BPA, said to contribute to only 1% of the total exposure for young children (Wilson et al. 2007). Despite the fact that these pathways do not

contribute to as much BPA exposure as dietary sources, the exposure from dermal and inhalation routes may be even more hazardous to the human body. BPA exposure by inhalation, dermal absorption, and subcutaneous exposure from medical applications bypass the liver's first-pass metabolism and go directly into the circulatory system. With the human body's filtering system being circumvented, greater harm could possibly be occurring from smaller doses (Vandenberg et al. 2007).

Research is currently uncertain of how these exposures affect the human body, but rat models with similar exposure pathways show health effects at low doses. Although there is little certainty of the health effects in the human body, the precautionary approach should be adopted to protect vulnerable populations from dermal and inhalation exposure to BPA. The population most likely effected by high dermal and inhalation exposures is occupationally exposed workers. The National Toxicology Program's (NTP) Center for the Evaluation of Risks to Human Reproduction Expert Panel 2008 monograph believes there is "minimal concern for workers exposed to higher levels in occupational settings" (NTP 2008). A policy option is to promulgate BPA OSHA PELs to protect workers from overexposure.

Another susceptible population is premature infants who may have early life exposures to BPA from medical instruments such as plastic tubing and PVC plastic medical devices. In a recent study of premature infants that have received medical treatment in the neonatal intensive care unit, it was found that babies that received the most intensive care had an order of magnitude higher urinary BPA concentration than the general population (Calafat et al. 2009). A screening process should be developed to evaluate the BPA and EDC content of medical devices.

Grass Roots Advocacy Approaches

The grass roots efforts of citizens and advocacy groups have been main change agents in reducing BPA in the food system. Consumer demand for BPA-free products and advocacy actions for regulatory reform played essential roles in the FDA's decision to amend its regulations, removing the approval for polycarbonate infant and toddler feeding systems to contain BPA. This federal change occurred after many smaller, hard fought battles to ban BPA in baby bottles occurred at the city, county, and state levels. Leadership was shown to protect infants and children from BPA in the food system through bans in Chicago, IL, Washington, D.C., Suffolk County, NY, Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, and New York. California also passed a ban, set to take effect after the federal amendment was already placed. The federal government ultimately responded to a petition from the American Chemistry Council that requested them to change the regulations (Federal Register 2012). This amendment did not reflect the FDA's change of opinion on the hazard of BPA; it was a reactionary move to re-align its regulations with the current industry practices. Industry had already removed BPA in its polycarbonate baby bottles and toddler drinking cups to meet consumer demand.

The baby bottle example shows how changes in consumer demand are a highly motivating factor for industry, sometimes more than legislative mandates. With this knowledge, it is opportune to apply these strategies to reduce BPA in the rest of the food system. Efforts that advocacy groups could take can be in a step-wise approach. The next "low hanging fruit" are foods that are consumed by infants and children. This includes the removal of BPA from infant formula cans, baby food jar lids, and other foods

marketed to children. Consumer boycotts followed by major retailers pulling these products off of the shelves, the same effective strategy taken for BPA in baby bottles, could work again for this effort. The consumer outcry could force companies to remove the BPA from these packaging, again, leading to the FDA making another after-the-fact amendment to their regulations. A parallel avenue that could be taken is for the advocacy groups to petition the government. Although the NRDC's BPA ban was not successful itself, it served the purpose of bringing mainstream media attention to the issue. This effort could elevate consumer awareness and lead to more universal boycott of these products.

Another effort that could be taken on by consumers and advocacy groups is the demand for transparency in food packaging chemicals. Current legislation allows manufacturers to keep their packaging formulations as trade secrets. An example of how strongly protected the manufacturers are with their proprietary formulas is the case of Eden Foods. Eden Foods contacted the manufacturers supplying their own cans for eighteen months. They were never successful in obtaining composition information for cans that they were using for packaging their own foods. A caveat in this law is that in some states labeling of products is required if the chemicals are listed on certain hazard lists, such as California's Proposition 65 List for chemicals known by that state to cause cancer or reproductive harm, even if it is a proprietary ingredient. After years of review and debate among agencies, chemical industry lobbyists, and advocacy groups, on January 25, 2013, California's Office of Environmental Health Hazard Assessment announced the intention to list BPA on the Proposition 65 list due to its reproductive harm. Only a thirty day comment period remains until final listing (OEHHA 2013).

Listing BPA on Prop 65 is a mark of progress even though labeling will only be required if a product exceeds the maximum allowable dose limit, or MADL, of 290 µg/day, an unlikely exposure level for a canned product.

With the knowledge about trade secret laws, advocates could address the issue of improved product labeling from two approaches. The first method would be to petition the state and federal government to move forward in requiring BPA to be listed on toxic chemical lists. For example, in California the NRDC petitioned CalEPA to re-review the science. It took years, but the efforts of this science-based advocacy group are finally coming to fruition. At the federal level, EPA would need to be lobbied to complete its rulemaking efforts to list BPA on the TSCA Concern List. The government could also be lobbied to require companies to label products that contain suspected endocrine disrupting chemicals.

The second method, in lieu of government support of improved labeling, would be to pressure companies to disclose information voluntarily about BPA content or endocrine activity. Pressure could be applied from two angles. The first angle would be to organize boycotts on products that do not disclose their packaging information. The second angle would be to boycott products that are labeled as containing BPA. These approaches force change because they affect sales, giving the product manufacturers the motivation they seem to be missing in the current regulatory climate. In an echoing statement, a packaging industry article reviewing the industry's stand on finding alternatives BPA remarked "if there is a sense of urgency at North American food and beverage companies and involved packaging suppliers to find and use BPA alternatives, they mask it well" (Packaging Digest 2012a). Without government intervention, the can

manufacturers are content to investigate alternatives at a casual pace. Without consumer boycotts, there is no incentive to change this current direction. As the consumer outcry of BPA in baby bottles issue displayed, a wide spread consumer boycott of products can start the chain reaction needed for industry and government to remove approval for BPA from packaging. Consumer demand has proven to be effective in changing the packaging in industry in other countries. In Japan, the consumer demand drove industry to make changes. The canning industry changed their can linings and polycarbonate dishes were pulled from schools. These efforts were made without government mandates requiring industry to make changes.

United States Government Policies and Scientific Opinion on BPA

FDA's latest action was to remove the approval for polycarbonate plastic for use in infant feeding systems. This effort was an alignment with current industry actions and did not reflect actions or changes of opinion on BPA safety by the FDA. Beyond polycarbonate baby bottles and sippy cups, FDA's current stand on BPA, as expressed on their web-site, states that there is "some concern about the potential effects of BPA on the brain, behavior, and prostate gland of fetuses, infants, and children." It conveyed reluctance to take a firmer stand on BPA because the agency's review of the weight of evidence did not demonstrate consistent and conclusive about the negative impact of BPA (FDA 2012c). FDA continues to support further research on BPA, a shift to a more robust regulatory framework, and a reduction in consumer exposure.

The U.S. EPA developed an Action Plan for BPA in March 2010. As part of the plan, the agency expresses intent to consider adding BPA to the TSCA Concern List. The Concern List is a list of chemicals to which the agency "finds that the manufacture, processing, distribution in commerce, use, or disposal, or any combination of such activities, presents or may present an unreasonable risk of injury to health or the environment" (EPA 2012b). The agency will initiate TSCA rulemaking to investigate the environmental presence and effects of BPA. If this rulemaking is completed, the agency could regulate BPA's use and disposal more stringently. The agency will also work with the EPA Design for the Environment program to investigate alternatives to BPA use in thermal receipts. The BPA Alternatives in Thermal Paper was issued in July 2012 and was open for comments until October 2012. The final part of the action plan is that the agency intends to work with the FDA, CDC, and NIEHS to better determine and evaluate

the human health impacts of BPA exposures. The Action Plan also stated that its focus is on environmental presence and environmental effects of BPA. Its aim is not to investigate human health issues.

EPA's most recent legislative action for BPA had been the issue of an Advanced Notice of Proposed Rulemaking (ANPRM) in July 26, 2011. In the ANPRM, the EPA requested comment on "requiring toxicity testing to determine the potential for BPA to cause adverse effects, including endocrine-related effects, in environmental organisms at low concentrations" (EPA 2013b). The EPA also sought comment on requiring environmental testing for BPA in water and soil to measure the amount of BPA the biota is being exposed to compared to points of departure for adverse effects, including EDC effects. The ANPRM was only intended to evaluate environmental sources and effects of BPA. The ANPRM was not intended to investigate additional testing for human health effects of BPA. The ANPRM comment period ended on September 26, 2011. There has not been a final rulemaking decision as of January 2013.

Although agencies are working on reviews of published literature, they have not taken an active stand on risk mitigation. In contrast, Health Canada has published a publicly available risk mitigation strategy. Health Canada's official evaluation of the risk stands pretty equally with the United States, believing that the science is not definitive about low-dose risks. The divergence occurs as Health Canada clearly states that it supports taking a precautionary approach to limit BPA exposures. It has added BPA to the List of Toxic Substances to allow better government control of use and disposal of BPA. For foods intended for newborns and infants, the government has adopted the as low as reasonably achievable (ALARA) principle. The government will aim to prevent or

minimize environmental releases of BPA. In addition, BPA will be added to the Canadian Total Diet Study so that exposures from foods can be better characterized (Environment Canada and Health Canada 2008b).

Scientific Research Approaches for Regulatory Reform

BPA's ubiquity in products and the environment and the ease of measuring its presence in the human populations has led it to be one of the most studied endocrine disruptors. While animal toxicity testing of BPA is prolific, current epidemiologic research is restricted to mostly cross-sectional studies and studies of small populations (Hatch et al 2010; Lang et al. 2008; Melzer et al. 2010; Melzer et al. 2012). With this limitation, the most salient question, what is BPA's role in causing health effects in humans, remains unanswered.

Stronger epidemiological data could help inform efforts to better regulate endocrine disrupting chemicals. Nationally representative studies, such as NHANES, could be enhanced to collect information critical to informing BPA dose response relationships. The foundational pharmacokinetics studies have been focused on studying healthy, young adults (Arakawa et al. 2004; Teeguarden et al. 2011; Volkel et al. 2002; Volkel et al. 2005). Detailed food packaging information and better timed urinary sampling could improve this field's understanding of how BPA is metabolized in the general population. These data could additionally work to assist in quantifying the portion of the aggregate exposure stemming from the food system. Some studies believe that the non-dietary exposures are contributing more than currently estimated (Christensen et al. 2012; Stahlhut et al. 2009). This expanded data and laboratory collection could contribute to modeling how much of the total exposure is from dietary sources.

The National Institute of Environmental Health Sciences (NIEHS) and the National Toxicology Program (NTP) have coordinated a consortium research effort to fill

research gaps. The efforts include intramural, extramural, and grantee consortium activities (Birnbaum et al. 2012). Their efforts are undoubtedly moving the science forward. What continues to be missed in the research efforts is a longitudinal epidemiological study. This type of study enables research to prove causality of BPA exposures to adverse health effects. Opportunities to study these effects are a couple of large scale longitudinal studies currently taking place in the United States. The Sister Study focuses on examining the environmental factors leading to breast cancer by studying a sister who has not been diagnosed with breast cancer and comparing their environment to the sister with breast cancer. This study, that aims to look at environmental endocrine disruptors, would be a good fit for the suggested dietary assessment methods to be implemented. The current National Children's Study is another longitudinal study that could benefit from examining the connections of dietary BPA exposure and dose, especially considering the importance of prenatal and early childhood exposures to endocrine disrupting hormones. It is unethical to conduct dosing study for this population, so utilizing this closely monitored observational study would be the next best method for improving the knowledge base on dietary BPA exposures.

Summary of Policy Recommendations

The decades of persistent work by scientists and advocates may finally be eroding long-standing regulations. The government seems to be awakening to the idea that change in regulations needs to take place for EDCs. The EPA acknowledged this need with an announcement in December 2012 stating its new effort to re-evaluate endocrine disrupting chemicals. The task force's specific mission is to review the latest low dose EDC studies to inform the EPA how to properly perform safety assessments for this class of chemicals. The difficulty of regulating endocrine disrupting chemicals is that they do not obey traditional toxicological paradigms. EDC's rarely follow a linear dose response or follow established and documented receptor pathways. Moreover, when EDC's enter the body, they are mixing with endogenous hormones already circulating in the body. A state of the science paper is slated for completion by the end of 2013 (EPA 2012c).

Instead of using the precautionary approach as Japan and Canada have chosen, the United States has remained largely paralyzed in its actions. With the exception of the amendment to remove the use approval of BPA in baby bottles and sippy cups, FDA regulations to reduce or remove endocrine disrupting chemicals from the food system are absent. The EPA's regulatory actions have been stalled at the ANPRM stage since 2011. Even though BPA is one of the most widely studied endocrine disrupting chemical, questions still remain about BPA's metabolism, receptor pathways and health effects in humans. The challenge is that these questions may never be definitively answered in the manner that the regulatory agencies expect. Although adverse effects have not been reliably reproduced, the numerous studies showing adverse effects indicate that BPA is capable of harm. There may not be a time in the near future when all of the questions

have been answered. The United States government should not use this shroud of uncertainty to enable inaction. Instead, the occupational, environmental, and health agencies should take strides to reduce exposures to endocrine disruptors to the United States population.

In summary, this policy analysis has suggested actions to reduce BPA and EDC exposure to the United States population. For food contact materials policies, testing standards need to be aligned with low dose effects of EDCs and focus on reproductive toxicity, developmental toxicity, and the toxicity of mixtures. Data from FDA monitoring of EDCs in food should be publicly released. Their research should include an investigation of sources of BPA in fresh foods. The FDA should begin to regulate BPA according to current food contact materials regulations and seek BPA free alternatives to canned food linings. Other steps for FDA would be to establish a protocol for estrogenic activity testing that is consistent and accurate. The trade secret protections of manufacturers in regard to EDCs should be amended.

For grass roots and consumer advocacy groups, their actions should focus on reducing BPA and EDCs in the food stream for infants and children. This effort should aim at removing EDCs from infant formula cans, baby food jar lids, juice boxes, and other packaged foods marketed to children. There needs to be a push for greater transparency in food packaging components. Lobbying efforts could be launched to demand manufacturers to disclose information and the government to require manufacturers to list EDC's used in food packaging on labels. Consumer boycotts should be enacted for canned foods and beverages that contain BPA.

Priorities for additional governmental efforts include movement forward by EPA on listing BPA on the TSCA Concern List. The EPA should revise the testing protocol for establishing safe levels of exposure, such as the Reference Dose, accounting for low dose and NMDRC health effects of EDCs. Vulnerable populations need to have better protection from inhalation and dermal absorption exposures. Occupational exposures could be protected by OSHA PELs for BPA. Medical devices need to be screened for estrogenic activity to prevent the known exposures of premature infants to BPA and EDC leaching from instruments during intensive care procedures. As governmental agencies continue to review the state of the science for BPA and EDCs, a move forward would be for the EPA to outline a risk mitigation strategy for BPA employing the precautionary principle.

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CHAPTER SEVEN: Conclusion and Next Steps

The aim of this dissertation was to explore the food system's contributions to bisphenol-A exposures through an analysis of dietary data and school meal exposure modeling. Since diet is the main pathway for BPA exposure, this research added to an important body of work examining sources of BPA exposures to inform intervention strategies aimed at reducing the body burden of this chemical. This final chapter will review the research contributions of these two projects and discuss directions for future research and policy actions.

Contributions from the NHANES Dietary Assessment Research

In an effort to create a greater knowledge base of BPA epidemiologic data, a novel method for analyzing dietary and biological NHANES data was applied. This research project aimed to identify the dietary contributions that can be associated with the highest BPA concentration levels in humans. Its regression models focused on relationships between urinary BPA concentrations and consumption of canned food and beverages, as identified by 24-hour dietary recall, accounting for demographic and socioeconomic factors. In addition, factor analysis methods were conducted to discover dietary patterns associated with higher urinary BPA concentrations.

The analysis of NHANES 2003-2008 datasets discovered greater consumption of canned food is associated with greater urinary BPA concentrations. More specifically, the multiple linear regression models revealed a statistically significant increase in urinary BPA concentration when consumption of canned pasta, vegetables, and beans increased.

Factor analysis methods were applied to seek dietary patterns of specific food groups that could be contributing to high BPA concentrations. The exploratory factor analysis revealed that the dietary patterns of the population with the highest urinary BPA concentrations differed from that of the whole population and the population with the lowest BPA concentrations. The dietary pattern differences in the highest decile give evidence that specific food groups could be contributing to higher BPA exposures.

Some areas of the research were limited because the food packaging of dietary recall items was not definitive. For example, when there was any doubt as to whether the food was canned, a conservative approach was taken that assumed the food was not canned. This weakened the analytical tools' ability to detect associations between canned food and urinary BPA concentration.

In order to strengthen the dataset's ability to identify BPA exposure sources and the body's response, an expansion of the collection of food packaging data and biological sampling is needed. Dietary recall data that include food packaging details and the correlated urinary BPA concentrations can provide dose response data from a nationally representative sample. It can also serve as the epidemiologic proof needed to strengthen the case of food packaging chemicals contributing to adverse health effects such as obesity, diabetes, and early puberty.

Contributions from the School Meal Exposure Studies

The school meal research modeled the potential daily dose of bisphenol-A from a typical breakfast and lunch of a school participating in the National School Lunch Program (NSLP) and the School Breakfast Program (SBP). Inputs to the exposure calculations were informed by formative research that used a mixed-methods approach including semi-structured interviews with stakeholders in school food service, ongoing communication with key school food partners, a food service director survey, school kitchen and cafeteria visits, and literature review for BPA food concentration values. The selected meal items and portion sizes followed the meal patterns of a public school that participates in the NSLP and SBP. Potential exposure to BPA in school meals was modeled in the range of 7.7×10^{-4} $\mu\text{g/kg-BW/day}$ for the minimum low exposure breakfast for a 6th-8th grader with average plate waste to a high of $0.97 \mu\text{g/kg-BW/day}$, for the maximum high potential exposure meal consumed during lunch for a K-5 student. Most of the modeled exposures were in the middle, in the range of 1 to 2×10^{-2} $\mu\text{g/kg-BW/day}$. The modeled daily doses were low in comparison to the reference dose (RfD) of $50 \mu\text{g/kg-BW/day}$, the dose considered to be safe for daily exposure over a lifetime.

Normally an exposure of 50 to 10,000 times lower than the RfD, the dose determined by the EPA to be safe, would be considered of negligible risk. For BPA though, there is debate about the applicability of the current reference dose. The RfD was based on a handful of high dose toxicity studies performed by private, industry funded laboratories. In addition, the use of high dose toxicity studies for setting safety standards may not be appropriate for use with endocrine disrupting chemicals (EDCs) that potentially display non-monotonic dose response. Low dose toxicity studies are

particularly important for BPA since EDCs often cause health effects at low doses that cannot be observed during higher dose exposures that are traditionally used in toxicology testing. Chronic, low doses also represent the typical human exposure to BPA. Another point to consider is that environmental EDC's are often entering systems where endogenous chemicals are already circulating, making the application of threshold linear dose response models for EDCs problematic.

Low dose studies of BPA have shown adverse reproductive development effects at the $\mu\text{g/kg- BW/day}$ exposure level. If one then selects a safety factor of 1000, as was applied to the LOAEL when the current BPA RfD was established, the safe exposure dose would be in the ng/kg- BW/day range. The doses modeled in this school lunch research, mostly in the range of 1 to $2 \times 10^{-2} \mu\text{g/kg- BW/day}$, were above this safe range. With this new point of comparison, the BPA exposure levels of school lunches do present a significant risk. This exemplifies the need for the current RfD to be revised and aligned with low dose toxicity studies.

The food service director survey, the school nutrition services field research, and the exposure modeling efforts confirmed the need for more studies of BPA in institutional food. Research should focus on laboratory analysis for BPA in foods unique to schools, such as institutional sized cans, bulk bags of frozen, pre-cooked proteins, and individually wrapped foods. Additional research should investigate the transfer of BPA from food preparation activities including the use of plastic cutting boards, application of plastic cling wrap directly onto foods, microwaving in plastic containers, and storing food in plastic vessels. Attention should also be focused on the migration of BPA from serving dishes and utensils, including plastic trays, paper wrapping, and paperboard serving trays.

BPA exposure from school meals can only be accurately characterized with the appropriate BPA data inputs. Exposure research should include breakfast and lunch, as the serving of both meals is now prevalent in schools.

To address findings of the school meals research, an educational campaign should be developed to elevate the awareness of food service directors about the migration of EDCs from food packaging and of the dangers of EDCs to the developing body. Serious chronic issues such as childhood obesity, diabetes, and early puberty can be linked to early exposure to EDCs. As a marker of progress, a section about chemicals in food and adverse health effects was included in Michelle Obama's national childhood obesity campaign, Let's Move. Their official report states "it is possible that developmental exposure to endocrine disrupting chemicals (EDCs) or other chemicals plays a role in the development of diabetes and childhood obesity" (White House Task Force on Childhood Obesity 2010).

As more research emerges on the connection between EDCs and diabetes and childhood obesity, focus needs to be aimed at the re-haul of the environmental health of school meals. One strategy could be to make incremental changes that work within the current school meal system. These smaller improvements could include substituting canned food for frozen or fresh, replacing the storage of food in plastic containers with stainless steel containers, and the use of more whole foods in salad bars.

For a more extensive reduction of endocrine disrupting chemicals in the school systems, fundamental changes need to take place. A holistic view should be applied about the exposure entry points of EDCs into the food system. Not only does the use of pre-packaged foods need to be limited, food should be served from stainless steel containers

and onto ceramic dishes or stainless steel. This drastic change for most schools would require complete renovations of warming kitchens and re-training of staff about scratch cooking. Other options would be a central district kitchen or contracting to health conscious school meal caterers to prepare meals for the district.

To enact these fundamental nutrition services changes, sustainable systemic shifts in how school meals are viewed in the educational system may need to take place. An apt observation representing the difference in how the United States school food system differs from the Japanese system was described recently in the Washington Post. When a Japanese government director of school health education attended a school lunch program meeting in Moscow, he noticed that the Japanese delegation was from the education ministry, whereas the other nation's representatives were from the agricultural and farm agencies (Harlan 2013). School meal programs would be drastically different in the United States if they were a part of the educational system. This could cause radical positive change in terms of funding and the school leadership's view of school meals. With elevated importance of the school meal, budget restraints could be lessened, more time could be allotted for eating meals when they are considered part of the curriculum, and educational lessons and community service projects could be developed supporting school food.

Policy Implications of the Research

In the policy analysis of BPA in the food system, it became clear that the challenges in properly regulating BPA stem from the premise that BPA is being governed as any other chemical, and not an endocrine disrupting chemical. This research suggests that for BPA to be effectively monitored in the food system, a paradigm shift of the regulatory framework needs to occur to account for the many different characteristics of the EDC class of chemicals.

There is a need for an overall push of endocrine disruptors and their contamination of the food system to the forefront. Endocrine disrupting chemicals can be found in soil and water, concerning the agricultural sector of the food system. Use of plastic tarps during cultivation has also been suggested as a source of BPA entry into the food system. EDCs can also be introduced into the food stream during storage, transportation, processing, and packaging steps. Plastic exposure and plastic packaging seeps into every part of the food production system. Especially salient is that widespread food contamination is a type of exposure that applies to the whole population.

The government has escalated its efforts to understand human exposure to BPA. The NIEHS consortium research is currently investigating BPA pharmacokinetics from human dosing studies and BPA exposure assessment in the occupational setting (Birnbaum et al. 2012). An effort should also be launched to establish a longitudinal epidemiologic study focused specifically at environmental chemical exposures. The study should be nationally representative and include all ages. Previously, nationally representative BPA data collection from NHANES has been an additional feature to the study's main goal of dietary assessment. Due to this, the study was not properly designed

to collect the packaging data needed to make the exposure dose connections. The timing of the biological sampling does not support current knowledge of BPA's rapid metabolism in the body. Improvements in these two areas would bring the epidemiological database of BPA metabolism in line with what is needed to make informed decision-making.

In school meals, the key to changing school nutrition policy and enacting a national effort to eliminate BPA from food served to children, clear scientific proof that chemical exposures from school food are linked to childhood obesity, early puberty, and diabetes needs to be presented to government officials. This topic has made its appearance in the national childhood obesity campaign. This national recognition should be amplified and utilized to ensure that this topic remains a priority.

The largest challenge in reducing the primary cause of the BPA exposures in school meals, the systemic use of canned and pre-packaged foods, can only sustainably change when there is a fundamental change in how school nutrition is viewed within the educational system. School nutrition programs are administered through the USDA, making them susceptible to farm and agricultural lobbying. The school meal would benefit from being considered part of the education core. Until then, school meals will be caught up in the federal funding treadmill driven by commodities and efficiencies.

BPA's current regulation in the United States is based on an RfD that is no longer appropriate with the current state of scientific research on endocrine disrupting chemicals. The RfD is the fundamental building block for all other food contact regulations. When the RfD is improperly established, it causes a cascade of issues with the guidance based on the RfD. Once the RfD is adjusted appropriately, the food contact

materials regulations will have to be updated. The protocols and trigger points for toxicity testing in food contact material need to be appropriately set for EDCs that have low dose effects, reproductive and development effects, and often display nonlinear, no threshold characteristics.

Laboratory analysis for detecting BPA and EDCs in food contact materials needs to be improved. Research has shown that current testing protocols often fail to detect estrogenic activity present in plastic materials. Tests only searching for BPA may also easily miss other estrogenic compounds. In addition to testing for estrogenic activity, endocrine disrupting chemicals have also shown that they can affect androgenic activity. Diagnostic protocol needs to be designed to detect the breadth of endocrine disrupting activity potentially found in food contact materials (Yang et al. 2011).

Future Directions

Bisphenol A is the subject of intense research and media attention because of its potential health risks to infants and children, pervasive exposure, and ubiquity in humans. BPA is one of many xenoestrogens that can be detected in the body, as well as being one of many synthetic chemicals with endocrine disrupting properties. Endocrine disrupting chemicals are challenging to current regulatory frameworks that rely on high dose toxicity testing with linear threshold dose response and established receptor pathways to set safe levels. In many ways, BPA is a pathfinding chemical for endocrine disruptors, paving the way to innovative regulation to non-monotonic dose response curves and non-traditional receptor pathways.

Governmental environmental and health agencies continue to evaluate the weight of evidence of animal tests of BPA, often missing the mark by assessing with traditional paradigms. Through extramural scientific research and the educational efforts of advocacy groups, the agencies are slowly recognizing the need to shift their approaches to setting safety standards. New criteria for evaluating safety need to be established as well as the correlating regulations to determine the safe use of BPA and EDCs in food packaging.

Although movement towards reducing BPA in the food system is moving in the right direction with the removal of BPA from infant feeding systems in the U.S., the journey to this point has been treacherous, with adversarial debate among industry, government, scientists, and advocacy groups. The estrogenic properties of BPA have been known since the 1930's, yet it gained approval for use in food packaging. Its estrogenic activity was re-confirmed in 1993 with scientific experiments in polycarbonate

flasks. Even with solid evidence of BPA migrating from polycarbonate materials, it has required nearly twenty additional years of research and advocacy for the ban on BPA use in polycarbonate infant feeding systems to take place. In the end, the FDA responded to a petition from the American Chemistry Council to remove the approval of BPA in PC baby bottles and sippy cups to align itself with current industry practice. This illustration of the influence of industry on BPA matters is not an isolated incident. The BPA debate is riddled with instances where industry sponsored research has been incorporated into the decision making process. Some of the most influential examples are EPA's establishment of the RfD and the FDA's latest scientific opinions; both are grounded on industry science.

Continuing to regulate the use of BPA in this manner shows a clear sign that industry is leading the health and safety efforts in this country. The path forward indicates a need for change unprecedented by government's past performance in this subject. What is essential is true leadership in making precautionary risk mitigation strategies with the current science instead of relying on the crutch of imperfect science to support stances that decision making needs to wait. Endocrine disrupting chemicals have proven their harm to human health and the environment. The doses and the endpoints may not be definitive, but this unknown portion of the science does not warrant complete inaction.

Although the ban on polycarbonate plastic use in baby bottles and toddler drinking cups has taken hold in the U.S., the plastic industry will continue to fight any future BPA bans as it did in the past. The packaging market is sizable, equal in size with the pharmaceutical industry (Muncke 2009). Despite the efforts of industrial lobbyists,

progress has been made in removing BPA from the food system. The movement forward has been a collaborative achievement of non-federal scientists resolutely collecting evidence supporting the adverse health effects of BPA, as well as grass-root efforts and consumer demand to make these changes. They will hopefully be joined by government agencies in moving the efforts forward to reduce BPA and endocrine disrupting chemical exposures in the food system.

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EDUCATION

2009-2013 **Johns Hopkins Bloomberg School of Public Health**, Baltimore, MD

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1998-2000 **Johns Hopkins Bloomberg School of Public Health**, Baltimore, MD

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Bachelor of Arts

Environmental Science Major, Ethnic Studies Minor

PROFESSIONAL EXPERIENCE

2000-2008 **Intel Corporation**, Santa Clara, CA

Industrial Hygienist

- Characterized occupational hazards and devised control strategies in semiconductor research and development and manufacturing facility, research laboratories, and office environments
- Global industrial hygiene catalog manager for over 50 courses. Successfully managed IH courses through aggressive development roadmap and software management application transition
- Actively partnered with biomedical life sciences labs ensuring the maturation of the lab community's safety culture and communication

2000 **Baltimore Gas and Electric**, Baltimore, MD

Industrial Hygienist

- Designed and conducted exposure assessments for chemical and physical hazards in the field
- Prepared technical reports and communicated risks and control recommendations to employees and management
- Evaluated office environment for indoor air quality issues and workplace ergonomics
- Established a corporate-wide noise monitoring database

- 1999 **Indoor Air Quality Section of the California Department of Health Services, Berkeley, CA**
Research Assistant
- Authored a draft program plan to assess and manage indoor environmental quality in California schools
 - Developed a database to manage information on indoor air quality in schools
- Summer 1996 **San Francisco Bay National Wildlife Refuge, Newark, CA**
Wildlife Biologist Intern through the *U.S. Fish and Wildlife Service*
- Managed and performed habitat restoration and endangered species monitoring
 - Coordinated, trained, and supervised volunteers for vegetation management projects

RESEARCH EXPERIENCE

- 2010-present **Food System Contributions to Bisphenol-A Exposures**
Dissertation Research
- Examined the role of the food system's contributions to bisphenol-A (BPA) exposures through an analysis of dietary data, modeling of the potential BPA exposure from school meals, and a review of food contact materials policies. Its discoveries enhance the epidemiologic work examining sources of bisphenol-A exposures from the food system to inform and improve policy.
- 2009 **Investigation of Pesticide Residue Levels of Domestic and Imported Food**
Research Assistant, Johns Hopkins Bloomberg School of Public Health and the Center for a Livable Future
- Performed data analysis to estimate the quantity of excess pesticide residue that could enter the U.S. if exporters followed originating country requirements but not U.S. pesticide tolerances for the top 20 imported produce items based on quantities imported and U.S. consumption levels. Research identified the potential pesticide health effects of the top pesticide residues of imported produce.
- 2009 **Tire Derived Rubber Flooring Chemical Emissions Study**
Peer Reviewer contracted by the California Department of Public Health
- Reviewed research examining volatile organic compound (VOC) emissions for a wide range of TDR flooring products. The research project aimed to provide information relevant to identify chronic exposure to VOCs emitted from products, as well as the decline of emissions over time. Exposure scenarios for a set of indoor conditions were used to predict potential exposures and health risks of TDR-flooring products for a range of indoor applications.

TEACHING EXPERIENCE

2009 – 2010 **Johns Hopkins Bloomberg School of Public Health**, Baltimore, MD
Teaching Assistant
Graduate Course titled Food Production, Public Health and the Environment course; Fall 2009, Fall 2010

1996 - 1998 **Youth Science Institute, Los Gatos, CA**
Lead Instructor

- Presented hands-on science programs
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- Trained and mentored junior instructors

Winter, Spring 1996 **San Francisco Bay National Wildlife Refuge**, Newark, CA
Environmental Education Intern through the Student Conservation Association

- Responsible for preparing learning stations
- Lead field trip orientation activities for parents and educators
- Developed environmental education materials

Summer 1995 **Haleakala National Park**, Kula, Hawaii

Interpretation Intern through the Student Conservation Association

- Researched, prepared, and presented interpretive programs on the natural and cultural history of the park and Hawaiian Islands
- Developed educational materials for park
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Winter, Spring 1995 **Industry Initiatives for Science and Math Education**, Lawrence Hall of Science, Berkeley, California
Research Assistant

- Conducted research for an environmental education project that partnered San Francisco Bay Area industries with local educators

PUBLICATIONS

Journal Articles

Neff RA, **Hartle JC**, Laestadius LI, Dolan K, Rosenthal AC, Nachman KE. A comparative study of allowable pesticide residue levels on produce in the United States. *Globalization and Health* 2012 8:2.

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INVITED PRESENTATIONS

Hartle, JC, Lawrence, RS. (October 2012) *Food System Contributions to Bisphenol-A Exposures*. Poster presented at American Public Health Association Annual Meeting.

Hartle, JC. (October 2012) *Food Packaging and Food Justice*. Presentation and expert panel for Creating Common Ground Funders Gathering.

Hartle, JC. (October 2009) *How to Conduct an Oral History*. Invited speaker to Baltimore Food Ecology Documentary course at the Maryland Institute College of Art (MICA)

Hartle, JC, Torres CW. (June 2007) *Beyond R & D: Development of a Chemical Review Forum for High Volume Manufacturing*. Presentation for the Industrial Hygiene General Practice Podium at the American Industrial Hygiene Conference and Exposition.

FUNDING

2009-2013 **Center for a Livable Future Doctoral Fellowship**

- Full tuition, stipend, and research funding

1998-2000 **National Institute of Occupational Safety and Health Training Grant**

- Full tuition and stipend funding

PROFESSIONAL QUALIFICATIONS

Statistical analysis: STATA IC 11.2

Mapping/GIS software: ESRI ArcGIS 10

Risk Assessment/Exposure Modeling Software: Oracle Crystal Ball

Foreign languages: Spanish- conversational

HONORS and AWARDS

2006 American Industrial Hygiene Association Future Leaders Institute Selected Attendee

2001 Safety and Health Leadership Award for supporting the Green Cross for Safety Award, Intel Corporation

PROFESSIONAL MEMBERSHIPS

2005 - Present Certified Industrial Hygienist
2000 - Present Associate Member, American Industrial Hygiene Association
2010 - Present Special Health Worker Member, American Public Health Association

COMMUNITY INVOLVEMENT

2011- Present **Landels Elementary School**, Mountain View, CA

Classroom Volunteer

Community Asset Building Champion for Project Cornerstone

- A parent engagement program designed to create positive connections with youth in the community by volunteering in schools, reading specially selected books, and leading activities that help teach valuable lessons.

2010- 2011 **Bellows Spring Elementary School**, Ellicott City, MD

Classroom Volunteer

- Assisted the classroom teacher during language arts centers, lead reading circles, and supported enrichment activities

2002 - 2005 **Stipe Elementary School**, San Jose, CA

Volunteer teacher's assistant

- Developed and presented hands-on science lessons; assisted special needs students during primary teacher's lessons

Summer 2003 **Monster Diversity Leadership Program**

Science Mentor and Resume Developer

- Multi-campus three-day weekend events which focused on leadership and career development and provided attendees with the opportunity to network with some of the top employers in the country

2001-2003 **Boys and Girls Club's Computer Clubhouse**, East Palo Alto, CA

Student Mentor

- Inspired and guided young students in the development of technology-based creative projects, including making digital videos, designing webpages, conducting web searches, and composing music

1997 **Coyote Creek Riparian Station**, Alviso, CA

Volunteer Bird Bander

- Assisted in migratory bird studies by opening and closing mist nets, banding new passerine captures, and collecting data on newly banded and recaptured birds

1994 – 1995 **American Cancer Society, Santa Clara Valley Chapter**, San Jose, CA
Volunteer Data Entry Assistant

- Utilized office Educational Tracking System to monitor chapter's public outreach programs